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THE SPEED OF HEALING OF MYOCARDIAL INFARCTION

A STUDY OF THE PATHOLOGIC ANATOMY IN SEVENTY-TWO CASES

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INTRODUCTION

THE treatment of any pathologic process can be carried out intelligently and scientifically only when it is based on a thorough understanding not only of how the lesion develops, but also of the means by which it heals and the speed with which this healing takes place. It has been known for a long time that occlusion of a main coronary artery or of a large branch will produce an infarct in the myocardium. It is also a well-recognized fact that, if the patient continues to live, such an infarct will undergo a process of healing, consisting of removal of the necrotic muscle fibers and replacement of them by connective tissue which in time forms a firm, contracted, fibrous scar.

It is very difficult, however, to find in the literature any exact description of the details of this process and, particularly, any discussion of the speed with which healing may be expected to take place in the human heart. This study was therefore undertaken in the hope that conclusions could be drawn which would be of value in the treatment of myocardial infarcts.

LITERATURE

The literature on coronary thrombosis and myocardial infarction is very extensive and, therefore, practically impossible to review here in any detail. The process of healing has been studied both in human autopsy material and experimentally.

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It was not until 1880 that pathologists began to show any particular interest in myocardial infarcts and really to grasp their significance. Undoubtedly, isolated instances had been described before this time. In this year (1880), Weigert,[1] in a paper entitled "Ueber die pathologischen Gerinnungsvorgänge," showed that myocardial infarcts were analogous to infarcts occurring elsewhere in the body. He described both the gross and microscopic appearance of acute myocardial infarcts and said that the healing process consisted in the removal of the necrotic muscle and its replacement by granulation and, eventually, by scar tissue. He also knew that a fibrinous pericarditis and an endocardial thrombus were likely to occur and that these also might be transformed into scar tissue. In the same year, Ziegler[2] introduced the term myomalacia cordis, in referring to these lesions.

From this time on, as a result of further refinements in histologic technique, more details of the process were gradually learned, but very little attention seems to have been paid to the speed with which healing occurs. It was not until the publication of Levine's[3] monograph on coronary thrombosis, in 1929, that there was any detailed attempt to correlate the age of the infarct with the gross and histologic findings. From the cases in his series in which an autopsy was performed, 46 in all, he drew the following conclusions: (1) Necrosis of muscle is the predominating feature from the fourth day to the end of the third week; (2) repair by connective tissue is demonstrable on the sixth or seventh day, but this is not striking until the third week; (3) five weeks are required for cicatrization to develop to a sufficient extent to prevent rupture; and (4) firm healing by vascularized scar tissue may be observed eight weeks after onset.

Experimental coronary occlusion was attempted even before cardiac infarcts had been recognized at autopsy. The first of these attempts was probably in 1698, only about seventy years after Harvey's description of the circulation of the blood. In that year Chirac[4] tied the coronary artery of a dog and found that the heart stopped beating almost immediately thereafter. Similar experiments were described by Erickson,[5] in 1842, and by Cohnheim and von Schulthess-Rechberg,[6] in 1881. In all of these early experiments the animals survived only a few minutes, and the observations made on the heart were of necessity physiologic rather than pathologic. The last two authors did, however, note that the portion of the heart muscle nourished by the occluded blood vessel became at first pale and soon afterwards a more livid blue.

In 1893, Kolster,[7] using an improved operative technique and tying only a small branch of a coronary artery, was able to keep some of his animals alive for periods varying from one day to one year and five months. He described such artificially produced lesions in a series of 12 dogs and demonstrated that the infarcts may heal by a process

similar to that now known to occur in man. The infarcts that he produced were not, however, complete infarcts. This was probably because only a small-sized vessel was occluded. With the histologic technique which he used, a satisfactory interpretation of the details of the process of healing was impossible.

Baumgarten,[8] in 1899, published an excellent discussion of experimental coronary occlusion but devoted more space to the physiologic than to the morphologic aspects of the problem. He used both cats and dogs, ligating various branches of the left and right coronary arteries. In this way, he was able to discover which areas of the myocardium obtained their nourishment from these blood vessels. Gross and histologic descriptions were given of the lesions produced in eight cats and six dogs. The survival periods varied from twenty-two hours to seven months. The acute infarcts were described as white, or whitish-yellow, opaque, and flaccid. In only three cases were the infarcts hemorrhagic. At the end of two weeks they became white and began to contract, and at seven months the infarct was converted into a thin, white, semitransparent, glistening membrane. Histologically, coagulation necrosis was fully developed after twenty-four hours. At three days, leucocytic infiltration was found, and there were signs of connective tissue proliferation along the margins of the infarct. By the end of fourteen days, connective tissue with many capillaries traversed the whole infarct, and the necrotic muscle had largely disappeared. The next and oldest infarct described was not very satisfactory in that it was only partial. It showed normal muscle traversed by bands of connective tissue. No difference in the process of healing was noted in the two types of animals used.

By far the most thorough and satisfactory of the studies of experimental myocardial infarction was published by Karsner and Dwyer,[9] in 1916. In order that their observations can be compared with ours on human material, we will give them in some detail.

Dogs were used, and in each the descending branch of the left coronary artery was tied. The dogs were killed after various lengths of time, and in this way a graded series of infarcts was obtained. The ages of the infarcts were one-half hour, 12 hours, 1 day, 2 days, 3 days, 5 days, 6 days, 11 days, 14 days, 18 days, 61 days, and 70 days. Careful gross and microscopic descriptions of each stage were given.

Grossly, the first recognizable change was pallor of the affected area. The infarct became gradually more sharply defined. At two days, it seemed dry and granular, and, at three days, the center was mottled with dusky red areas while the endocardial and pericardial surfaces were a gray-yellow. By five days the infarct was sharply defined, somewhat thinned, and surrounded by a fine line of reactionary hyperemia. The eleven-day infarct was mottled yellow gray and dusky red and surrounded by a thin gelatinous border. At eighteen days this

border had become much thicker. The picture at sixty-one days was one of complete fibrosis, although minute yellow dots of necrotic material could still be seen. After seventy days only a fibrosed scar was found.

The histologic changes were as follows. In the earliest infarct, one about a half-hour old, ill-defined areas showing interstitial edema, congestion, and small hemorrhages were found. The cross striations of the muscle fibers were decreased. By twelve hours there were also areas of hyaline necrosis of the muscle fibers, pyknosis or disappearance of muscle nuclei, polymorphonuclear leucocytic infiltration, and a few mononuclear cells. In the twenty-four-hour infarct, hyaline necrosis of the muscle was increased, and these necrotic fibers were becoming fragmented and invaded by polymorphonuclear leucocytes. Also, the connective tissue around the blood vessels and beneath the endocardium contained mitotic figures. These fibroblasts had noticeably increased in number by forty-eight hours, and after five days there was a well-defined zone of these cells at the periphery of the infarct. At six days definite plasma cells were found among the infiltrating cells. From eleven to eighteen days, the necrotic muscle gradually decreased in amount and was slowly replaced by connective tissue. Mitotic figures in the fibroblasts gradually decreased in number. At eighteen days the infarct had become a well-defined scar, although necrotic muscle, monocytes, polymorphonuclear leucocytes, and lymphocytes were still present. Very small areas of necrotic muscle were still present at sixty-one days and seventy days, but the connective tissue had become very much condensed and the cellular infiltration had disappeared.

From the preceding discussion it can be seen that, save for the descriptions given by Levine, the only work that has taken the time element in healing into consideration has been carried out on experimental animals. The pathologic discussion given by Levine, although excellent, does not cover a sufficient number of cases and is not detailed enough for adequate conclusions. The experimental studies allow one to conclude that infarcts similar to those seen in man can be produced in animals, and that these infarcts heal by a process very like that which occurs in the human. It does not seem fair to state, however, that this process goes on at the same speed as in man, for it is obvious that the infarcts in the animal must be smaller because of the small size of the heart itself, and also that the remaining collateral circulation in the animal heart is relatively more adequate because no marked degree of arteriosclerotic change is present.

MATERIAL OF PRESENT STUDY

The material used in this investigation consisted of patients who showed a myocardial infarct at autopsy and had been thoroughly

studied clinically, so that conclusive evidence as to the onset, and therefore the age, of the infarct was available. In order to obtain an adequate number of such cases it was necessary to use material from several hospitals. We are grateful to the following Boston Hospitals for their aid in this study: Peter Bent Brigham, Beth Israel, Boston City, and Massachusetts General.

Although the original group consisted of more than 100 cases, only seventy-two of these were found to be entirely satisfactory from all points of view. The distribution of these cases from the standpoint of the age of the infarct can be seen in Table I. As is shown by this

TABLE I

AGE DISTRIBUTION OF THIS SERIES OF MYOCARDIAL INFARCTS

FIRST WEEK		SECOND WEEK		THIRD WEEK		FOURTH WEEK	
DAYS	NO. OF CASES	DAYS	NO. OF CASES	DAYS	NO. OF CASES	DAYS	NO. OF CASES
1	11	8	0	15	0	22	2
2	5	9	3	16	1	23	2
3	3	10	3	17	0	24	0
4	2	11	0	18	2	25	1
5	2	12	2	19	0	26	2
6	2	13	1	20	0	27	0
7	2	14	2	21	2	28	1
Total	27		11		5		8*

FIRST MONTH		SECOND MONTH		FIRST HALF YEAR		SECOND HALF YEAR		YEARS	
WEEKS	NO. OF CASES	WEEKS	NO. OF CASES	MONTHS	NO. OF CASES	MONTHS	NO. OF CASES	YEARS	NO. OF CASES
1	27	5	3	1	55	7	0	1	66
2	11	6	1	2	4	8	0	2	1
3	5	7	0	3	1	9	0	3	1
4	12*	8	0	4	1	10	1	4	3
				5	0	11	0	11	1
				6	1	12	3		
Total	55		4	Total	62		4	Total	72

*The clinical age in 4 cases was given as one month.

table, a sufficiently satisfactory distribution of infarct ages occurred in the period of the first five weeks, but thereafter only more or less sporadic representation was found. Old, completely healed infarcts were also comparatively easy to find, and in some of these cases the age of the infarct could be computed from the history. It was very difficult, however, to obtain data from patients dying in the period of from six weeks to eleven months after the occurrence of the infarct.

The following general features of the group are of some interest, and, when compared with other larger series, show that our group was representative.

1. Age of patient. The average age of the patients was 59.2 years; the youngest was 42 years of age, the oldest, 79 years.

2. Sex. Seventy-four per cent of the patients were males and 26 per cent were females.

3. Weight of the heart. The average weight was 503.5 gm.; the smallest weighed 300 gm., and the largest, 880 gm. It was thought that the weight of the heart in relation to the age of the infarct might be of some interest. Four hearts with infarcts 1 to 2 months old averaged 450 gm. in weight, five hearts in which the infarct was 2 to 6 months old averaged 500 gm., and eighteen hearts in which the infarct was more than 6 months old averaged 570 gm. These data suggest that an infarct, per se, may lead to cardiac hypertrophy.

4. Cardiac rupture. This had occurred in eight cases. None of these infarcts was more than 2 weeks old. The average weight of these eight hearts was 484 gm.

5. Diabetes mellitus. This disease was present in nine cases. The average age at time of death in this group was 58 years.

6. Coronary arteries. In practically all of these cases there was a moderate to marked generalized coronary atherosclerosis in addition to occlusion of a branch. In the original group, definite thrombi were found in seventy instances. The distribution of these thrombi was as follows:

a. Left coronary artery	59	cases
Descending branch	52	
Circumflex branch	4	
Septal branch	3	
b. Right coronary artery	8	cases
c. Right and left coronary arteries	3	cases

7. Location of the infarct. As would be expected from the location of the occlusions, the majority of the infarcts involved the apex of the left ventricle alone, or this and the interventricular septum. In fifty-four of the cases the location of the infarcts was described in sufficient detail so that a satisfactory idea of their position and extent could be obtained. The distribution of these is given in tabular form below:

Left ventricle	
Apex	24
Apex and septum	22
Base	5
Base and septum	2
Right ventricle	1

8. Valve lesions. Aortic stenosis, probably caused by arteriosclerosis, was present in four cases, and in one there was a rheumatic mitral stenosis.

In many of the cases the only histologic material available consisted of the routine autopsy sections of the heart. Most of these had been stained with phloxine methylene blue, a few with hematoxylin and eosin. Material fixed in Zenker's fluid and in formalin was, however, obtainable in the cases representing the more important ages of the

infarct, and in these cases phosphotungstic acid hematoxylin, aniline blue connective-tissue, iron, and fat stains were made.

The histologic changes will be first described and then correlated with the gross appearances. In dealing with the histologic picture, a discussion of the appearance and progress of each of the histologic features will be first presented, and then an attempt made to describe the criteria characteristic of the various ages of the infarcts.

HISTOLOGIC DATA

Necrosis.—The first result of a stoppage of the blood supply to a portion of the myocardium is necrosis of the muscle fibers and, to a lesser extent, of the connective tissue and smaller blood vessels. Although probably the necrosis of the muscle starts almost immediately, it is difficult or impossible to find any definite histologic evidence of it until five or six hours have elapsed. There are several changes that then become evident. The most striking and generalized of these is that the involved muscle fibers begin to appear somewhat hyaline and take a much deeper acid stain. In a hematoxylin and eosin, and, to a much more marked extent, a phloxine methylene blue preparation, they are a much brighter red. The striations become somewhat more difficult to see, but do not disappear, and can even be found in later stages when the muscle fibers have been broken into small fragments and have undergone phagocytosis by histiocytes.

Other signs of necrosis occur in single fibers or small groups of fibers. In these the striations cannot be made out; the fibers are swollen and contain eosinophilic granules of various sizes, or large, irregular cross bands.

If the thrombosis is complete the necrosis will be found to occur uniformly throughout the infarct, save for a thin layer of surviving tissue along the endocardium which extends along the Thebesian veins up into the myocardium. This layer is about 0.3 to 0.5 mm. in thickness. Its existence must be explained by assuming that nourishment passes directly through the endothelium from the blood present in the lumen of the ventricle and in the veins. It was also found to occur in the experimental infarcts described by Karsner and Dwyer.

Necrotic muscle is a constant constituent of these infarcts and, although gradually removed, may persist for a long period of time. It was found in two out of five infarcts at 1 month of age, in two out of three at 5 weeks, in one at 6 weeks, and in one at 4 months.

Hemorrhage.—Hemorrhage into infarcts is somewhat variable. It frequently occurs, but is usually found to be focal rather than spread diffusely throughout the infarct. On histologic examination, the erythrocytes are most frequently found to be in distended venules and blood capillaries, while true extravasation around the muscle fibers is comparatively rare. As these hemorrhages become older the erythrocytes

break up, and eventually the hemoglobin which they contained is taken up by macrophages in the form of hemosiderin. In the past there has been much discussion as to whether myocardial infarcts should be classified as anemic or hemorrhagic. The true answer to this question is probably that they may show features of both and are rarely, if ever, purely one or the other.

Fat.—The amount of fat present in an infarct is to a large extent dependent on how suddenly the thrombosis or occlusion took place. If the area of myocardium that is infarcted has previously had an insufficient circulation, fatty degeneration will have occurred, and the infarcted muscle contains a large number of small fat droplets. If, on the other hand, the muscle was entirely normal before it was infarcted, it shows only a small amount of fat. In this type of infarct the majority of the fat will be found on the periphery, adjacent to normal fibers, while the central fibers show little or none. The probable explanation of this distribution is that these peripheral fibers get partial, but insufficient, nourishment from the adjoining normal tissue. The amount of fat decreases as the infarct gets older and is removed at the same time as the necrotic muscle fibers.

Infiltration with Polymorphonuclear Leucocytes.—As a result of the necrosis of muscle, polymorphonuclear leucocytes are attracted and soon begin to infiltrate around and into the necrotic muscle. This apparently begins about as soon as signs of necrosis can be identified in the muscle. This infiltration starts peripherally and spreads centrally; it is much more active on the epicardial side and in those portions adjacent to the uninvolved muscle with intact vasculature than on the endocardial surface. In the earliest stages the polymorphonuclear leucocytes are found in the interstitial tissue and around the blood vessels. From here they infiltrate diffusely around and, to some extent, into the necrotic fibers. The power to penetrate seems somewhat limited, and in large infarcts, particularly when the remaining circulation is poor, the central portions of the infarct never become infiltrated. Sometimes a sharp line of demarcation can be found between the infiltrated areas and those that are not, suggesting that the infiltrative power of the leucocytes is definitely limited.

The first signs of infiltration are seen in infarcts during the first twenty-four hours. The amount of infiltration progressively increases during the first four days. At about forty-eight hours some of the polymorphonuclear leucocytes start to undergo degenerative changes, as evidenced by the loss of sharpness of their outlines and the accumulation of fragments of nuclear debris. By the fifth or sixth day many of the polymorphonuclear leucocytes have become necrotic and thereafter gradually disappear. By the fourteenth day they have practically completely disappeared.

For some reason not understood, after the removal of the peripheral muscle fibers, in the process of healing, the remaining central necrotic

muscle provokes little or no fresh infiltration of polymorphonuclear leucocytes, even when the collateral circulation has developed to such a point that fresh capillaries are present adjacent to it.

The exact function of the polymorphonuclear leucocytes is difficult to explain. They do not phagocytose the necrotic muscle. It is possible that they may produce some enzyme which aids in the final breakdown and phagocytosis of the muscle fibers, but they produce no definite change in the muscle fibers that can be recognized histologically.

Infiltration by Eosinophiles.—From the fourth to the eighteenth day, varying numbers of eosinophiles may be found in the areas of infiltration.

Ingrowth of Blood Vessels and Connective Tissue Cells.—Newly formed blood capillaries can be found growing into the infarcted area, beginning on about the fourth day. This process starts on the periphery and extends centrally. When the infarct involves the endocardial surface, only slight ingrowth of blood vessels and connective tissue can be found occurring from this side. The extent of this vascularization seems to be limited to a certain degree. It takes place quite rapidly on the periphery and more slowly in the center. In large infarcts which show necrotic central masses of muscle, frequently no vascularization of this tissue can be demonstrated even at periods when the periphery of the infarct is well healed. These newly formed blood vessels never seem to attain very large size.

Accompanying these blood vessels, fibroblasts can be seen to grow into the infarcted area. These frequently show mitotic figures. While still young, they show, in the phloxine methylene blue preparation, a basophilic staining of their cytoplasm. These basophilic fibroblasts have been found in infarcts ranging in age from 4 to 23 days.

It is very difficult to be sure whether all of the fibroblasts found in the healed stage of the infarct are the result of this ingrowth, or whether part of them represent the original fibroblasts of the stroma of the heart which have survived while the muscle fibers have not.

When one compares the healing of cardiac infarcts with the healing of infectious lesions, one discovers that the fibrin which is present in the latter is quite strikingly absent in the former. The ingrowth of connective tissue and blood vessels cannot be explained as an organization of fibrin; the exact stimulus for it is not known.

The Removal of the Necrotic Muscle, and Infiltration by Pigmented Macrophages.—The removal of the necrotic muscle is the result of phagocytosis by mononuclear cells, probably histiocytes. This process starts at the periphery and begins simultaneously with the ingrowth of blood vessels and connective tissue. The histiocytes penetrate the necrotic muscle fibers and gradually phagocytose the muscle. They can be found containing reddish fragments of muscle. These fragments are apparently dissolved in the cell, and they disappear. The waste, or

lipofuscin pigment of the muscle, is also phagocytosed, but it cannot be dissolved and remains in the cell. Because of this, any healing infarct can be found to contain numerous pigmented macrophages.

Most of the pigment in these phagocytic cells was formerly present around the nuclei of the muscle fibers. It is yellow-brown in color and does not give a positive iron reaction, but does stain faintly with scarlet red. Some of the cells, however, do contain iron-positive hemosiderin granules resulting from the breakdown of erythrocytes in hemorrhagic areas. Frequently both types of pigment are present in a single macrophage.

The removal of the necrotic muscle occurs much more rapidly at the periphery than it does centrally. In a 10-day infarct the peripheral muscle fibers are usually completely removed for a distance of about 1 mm. Active absorption can be demonstrated to be taking place in infarcts as old as 6 weeks. After this time necrotic muscle may still be present, but signs of absorption are difficult to demonstrate.

The pigmented macrophages remain for a time after actual absorption has ceased. As the infarct becomes older they decrease in number, and in infarcts 1 to 2 years old they have practically disappeared.

Lymphocytes and Plasma Cells.—Foci of lymphocytes and plasma cells can be found in infarcts as soon as absorption of muscle fibers starts. They are never as numerous as the macrophages. They also decrease in number as the infarct becomes older and usually disappear at about the same time as the pigmented macrophages.

Collagen Formation by the Fibroblasts.—As the newly-formed connective tissue in the infarct becomes older, increasing amounts of intercellular collagen fibers are formed. It is the formation of this collagen that increases the strength of the fibrous scar. Fine, newly-formed collagen fibers are usually found first at about twelve days. At three weeks the collagen is moderately prominent, particularly at the periphery, and at about two to three months it has reached its maximum.

The Pericardium.—In many infarcts, particularly those in which the muscle beneath the epicardium is involved, a fibrinous pericarditis can be found after twenty-four hours. This begins to become organized about the eighth or ninth day and, unless of unusual thickness, or-

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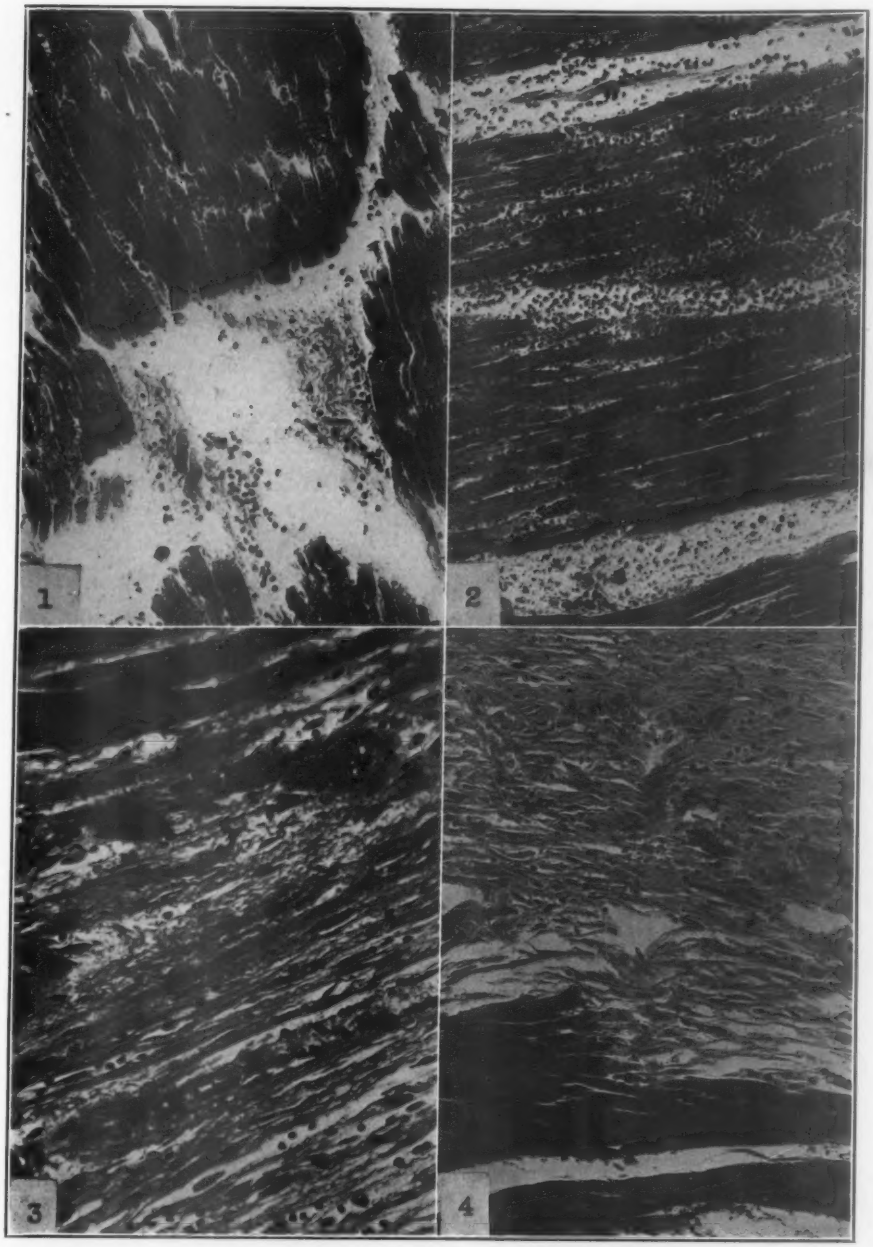
Fig. 1.—Photomicrograph, medium power, 24-hour infarct. The muscle fibers are swollen, opaque, and take an acid stain. The nuclei are difficult to make out. Many muscle fibers have a banded, granular appearance. There are a slight degree of polymorphonuclear leucocytic infiltration in the interstitial connective tissue and very early invasion between the muscle fibers.

Fig. 2.—Photomicrograph, medium power, five-day infarct. Necrosis of muscle fibers is shown by deep staining with eosin. Nuclei are difficult to make out. There is marked infiltration by polymorphonuclear leucocytes between, and, to a certain extent, into, the necrotic muscle fibers. Particles of nuclear debris in areas of infiltration have arisen as a result of the necrosis and breakdown of the polymorphonuclear leucocytes. There is periphery of infarct above and in central portion below. Infiltration tends to decrease toward center.



Figs. 1 and 2. (*See opposite page for legends.*)

Fig. 3.—Photomicrograph, medium power, fourteen-day infarct. Peripheral muscle fibers have been completely removed. Fairly numerous, fine collagen fibers are present. There is infiltration with pigmented macrophages and lymphocytes.

Fig. 4.—Photomicrograph, medium power, five-week infarct. Field chosen to show histologic picture adjacent to central necrotic muscle. No acute reaction is present. A few histiocytes appear next to the necrotic muscle fibers which are apparently phagocytosing them. Collagen is quite prominent except adjacent to the necrotic muscle. A few lymphocytes and pigmented macrophages are present.

ganization should be complete in about four weeks after the onset of the infarction. (See Table II.)

TABLE II

ORGANIZATION OF PERICARDIAL LESION

	UNORGANIZED	ORGANIZING	ORGANIZED
2 days	1		
3 days	2		
4 days	1		
5 days	2		
9 days		3	
10 days		1	
12 days	1	1	
13 days			2
23 days			1
26 days			8
1 month		1	

The Endocardial Thrombus.—In our experience, the occurrence and state of organization of an endocardial thrombus have proved less reliable than the pericardial reaction as a means of judging the age of an infarct. Endocardial thrombi occur as early as the fifth day. Beginning organization is found on the ninth day, and complete organization, on the sixteenth day. Fresh or only partially organized thrombi are, however, found in comparatively old infarcts. Because of this we feel that at least some of the mural thrombi occur, not as a direct result of the infarct, but as a secondary result of a later dilatation of the heart. This is shown in Table III.

TABLE III

ORGANIZATION OF MURAL THROMBUS

	UNORGANIZED	ORGANIZING	ORGANIZED
4 days	1	1	
5 days	2		
6 days	1		
9 days		1	
10 days		1	
12 days		2	
14 days			1
16 days			1
23 days		1	
26 days			1
4 weeks		3	
5 weeks		1	1
3 months		1	
10 months			1
3 years			1

CHARACTERISTIC FEATURES OF INFARCTS OF VARIOUS AGES

Even when one keeps the above-described criteria in mind, it is not always easy to judge the age of an infarct from the histologic section. This is particularly true of the infarcts that are three or more weeks old. To judge the age of an infarct, it is very important that the

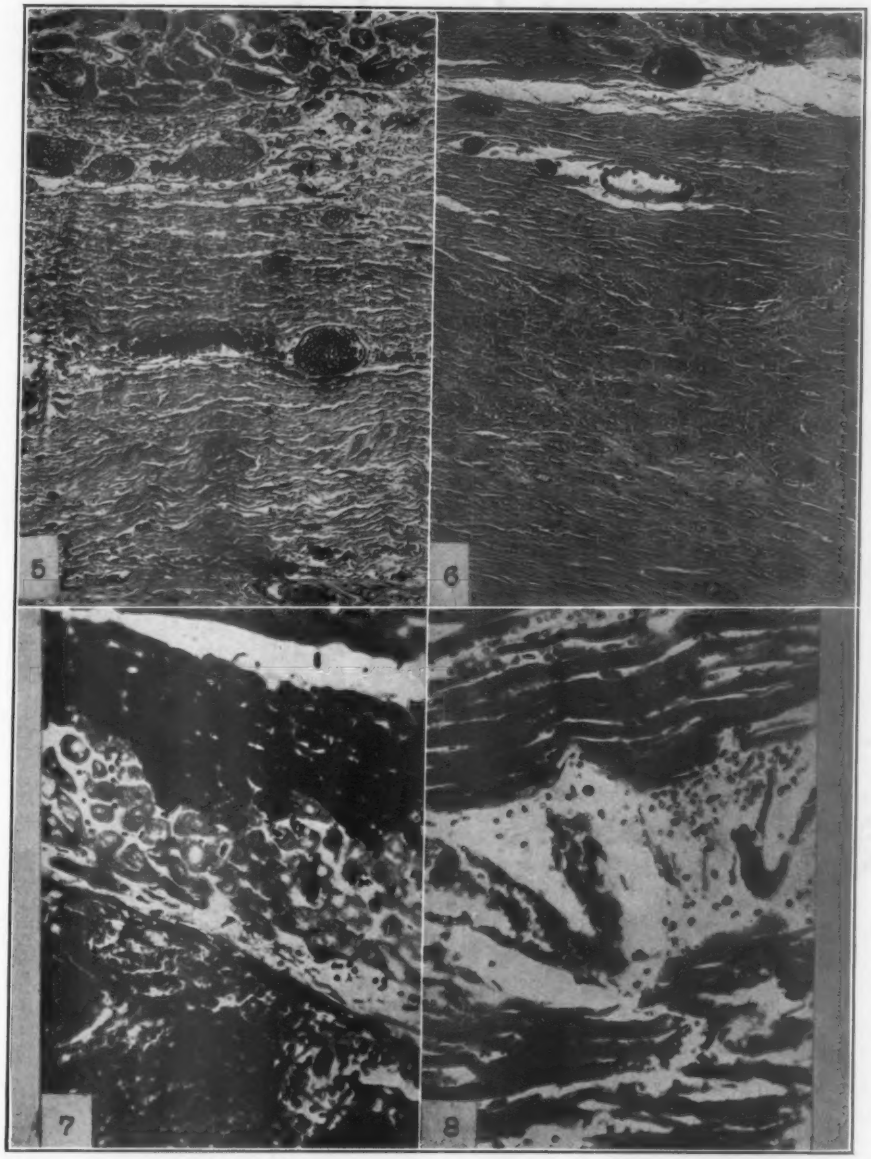


Fig. 5.—Photomicrograph, medium power, three-month infarct. Periphery is shown with normal fibers above. In the infarct, collagen has become very dense and prominent. The vessels are still moderately prominent. Infiltration of cells has practically disappeared.

Fig. 6.—Photomicrograph, medium power, four-year infarct. Normal muscle is shown above. Infarct consists of very old, dense, scar tissue. Little can be seen in scar but very thick collagen bundles. Cell nuclei are rare, and tissue is relatively avascular.

Fig. 7.—Photomicrograph, medium power, five-day infarct. Endocardial surface is shown. Below is an unorganized mural thrombus. There is a band of uninvolved muscle above this which has been spared as a result of obtaining nourishment from the ventricular cavity. Dark-staining necrotic muscle is above this. Note that practically no infiltration has occurred from the endocardial surface.

Fig. 8.—Photomicrograph, medium power, ninety-six-hour infarct. Periphery of infarct shows beginning proliferation of blood vessels. Small capillary sprouts can be seen growing in towards the infarcted area.

material for microscopic examination be taken from the proper area. As has already been pointed out, healing takes place at different rates of speed in various portions of the infarct. It is slowest in the center and most rapid at the periphery, particularly in those areas adjacent to the most effective collateral circulation. A section which shows both uninvolved musculature and the edge of the infarct is the most satisfactory.

When such a section is available one should be able to date infarcts with a fair degree of accuracy. The histologic features that should be found in the infarcts of various ages are the following:

First Week.—During the first twenty-four hours, necrosis of muscle should be found, with slight polymorphonuclear leucocytic infiltration at the periphery. From the second to the fourth day the degree of this infiltration should increase progressively. In the four-day infarct the periphery should show marked infiltration with polymorphonuclear leucocytes, with degenerative changes and signs of necrosis in many of those infiltrating cells. On the fourth or fifth day the first signs of removal of muscle fibers appear. Blood capillaries and connective tissue can be found penetrating the infarct from the periphery. Single fibers, or small clumps of fibers, may have undergone phagocytosis and removal by the seventh day.

Second Week.—It is during this stage that the removal of the peripheral muscle fibers becomes a prominent histologic feature. By the tenth day there is a peripheral zone, 1 mm. or more in thickness, from which the necrotic muscle fibers have been almost completely removed. As a result, numerous pigmented macrophages are found. The ingrowth of blood vessels and connective tissue has become quite prominent. The fibroblasts have a curious basophilic character. Moderate numbers of eosinophiles, lymphocytes, and plasma cells may be found. Active phagocytosis and removal of fibers occur along the edge of the remaining necrotic muscle. By the end of the second week the muscle fibers should be almost completely removed from small infarcts (3 to 4 mm. in diameter). Polymorphonuclear leucocytes have practically disappeared.

Third Week.—During the third week the removal of muscle fibers still continues in large infarcts. Pigmented macrophages are numerous. Eosinophiles are still present, but decreasing. The basophilia of the fibroblasts is also becoming less marked. Plasma cells and lymphocytes may be fairly prominent. In addition to these features, the first signs of collagen formation may be found in the form of fine collagen fibers. These are first produced by the fibroblasts at the periphery.

Fourth to Sixth Week.—During this stage, recognition of the age of the infarct is largely dependent upon the amount of collagen that has been formed by the connective tissue cells. Therefore, accurate dating

is difficult or impossible. A necrotic central mass of muscle may still be found during this period, and usually some signs of active removal of this material are still present. By the end of this period, collagen is quite a prominent feature in the infarct. The whole scar is definitely contracted, and the vascularity and infiltration by pigmented macrophages and lymphocytes are beginning to decrease.

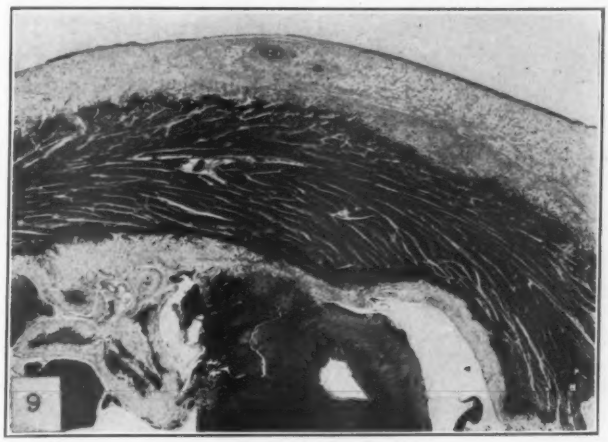


Fig. 9.—Photomicrograph, low power, ten-day infarct. Complete cross section of wall of left ventricle. Infarct has involved the whole wall. Dark-staining tissue in central portions consists of necrotic muscle fibers without reaction. Along both upper and lower borders of this is a narrow band in which the muscle has been almost completely removed, showing that healing is taking place from both endocardial and epicardial sides. A similar process can be seen in the papillary muscles, where dark-staining necrotic muscle is present in the central portions. There are present a fibrinous pericarditis and an endocardial thrombus, both of which show early organization.

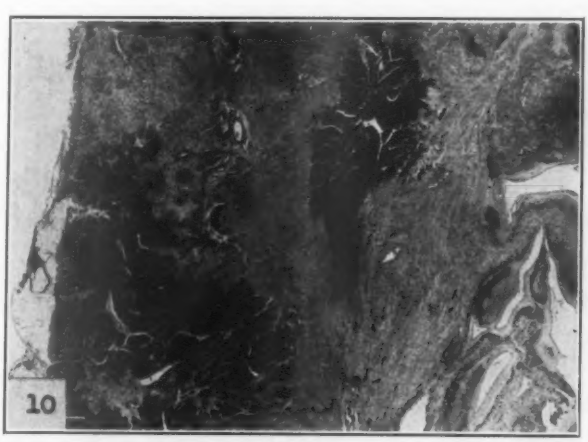


Fig. 10.—Photomicrograph, low power, sixteen-day infarct. Wall of left ventricle. A dark central area of necrotic fibers which are not as yet removed is shown. At upper left is a wedge-shaped area of uninvolved muscle. Pale areas are those in which muscle has been completely removed. Infarcted area has not yet shrunk appreciably. Note thin area of uninvolved muscle along endocardium. There is a completely organized endocardial thrombus at lower right.

Sixth Week to Second Month.—During this period the collagen becomes more and more dense, until, at the end of two months, this process has about reached its maximum. Except in very rare cases, the muscle fibers are completely removed by the end of this period. Cellular infiltration is markedly diminished. The infarct is now practically healed.

Second Month On.—Very little further change takes place, although some pigmented macrophages and lymphocytes may be found up to one year.

The findings described above are summarized in Table IV.

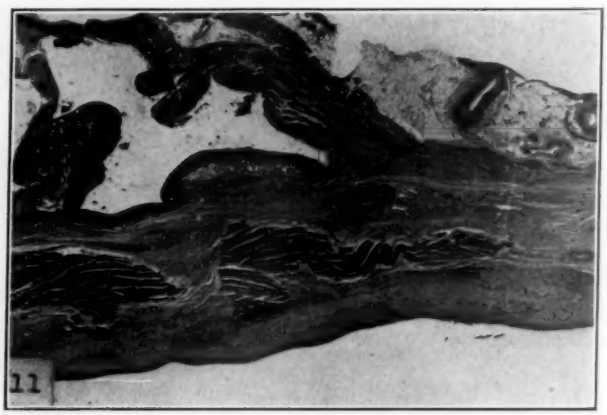


Fig. 11.—Photomicrograph, low power, five-week infarct. Central islands of necrotic muscle are still present. In areas surrounding these, muscle fibers have been completely removed. The scar is becoming dense and contracted. Note sharp areas of demarcation between necrotic muscle and healed areas. A dense, completely organized endocardial thrombus and marked sclerosis of blood vessels are present. In two areas which apparently have better vascularization, muscle fibers have been removed throughout the entire thickness of the myocardium.

GROSS APPEARANCE

Attempts were made to discover the gross characteristics of infarcts of various ages. For this purpose the only available material in the majority of the cases consisted of the gross descriptions given in the autopsy protocols. The results were discouraging, save for a few generalities. Most infarcts were described as soft, until an age of two to three months was reached. From that time on they were usually noted as firm and contracted. The descriptions of the colors were even less helpful. Most early infarcts were described as yellow, or red, or pale, and no uniformity was reached until the infarcts were about three months old, when they were depicted as white, fibrous scars.

As a result of these difficulties, myocardial infarcts from which gross specimens had been preserved and those occurring in current autopsies were observed, and the gross and microscopic pictures correlated. This series is as yet too small for entirely satisfactory conclusions. It is sufficient, however, to allow us to say that most of the

TABLE IV

TIME RELATIONSHIP OF VARIOUS HISTOLOGIC FEATURES OF MYOCARDIAL INFARCTS

	NECROTIC MUSCLE	POLYMORPHONUCLEAR LEUCOCYTIC INFILTRATION	BLOOD VESSELS AND CONNECTIVE TISSUE	REMOVAL OF FIBERS	PIGMENTED MACROPHAGES	EOSINOPHILES	PLASMA CELLS AND LYMPHOCYTES	COLLAGEN
1 day	++	+	0	0	0	0	0	0
2 days	++++	++	0	0	0	0	0	0
3 days	++++	+++	0	0	0	0	0	0
4 days	++++	++++	0	0	0	0	0	0
5 days	++++	++++	+	+	0	0	0	0
6 days	++++	+++	++	+	+	+	+	0
7 days	+++	++	++	+	+	+++	+	0
2 weeks	++	+	+++	+++	+++	++++	+++	+
3 weeks	+	+	+++	+++	++++	+	++++	++
4 weeks	+	0	++++	++	++++	0	++++	++
2 months	+	0	++++	+	+++	0	+++	+++
3 months	+	0	++++	+	+++	0	+++	++++
4 months	0 to +	0	++++	?	++	0	++	++++
5 months	0 to +	0	++++	?	+	0	+	++++
6 months to 1 year	0	0	++++	?	+	0	+	++++
1 year and over	0	0	++++	0	+	0	0	++++

features described histologically can also be seen grossly if the infarcts are examined closely enough.

The earliest change after infarction is that the involved area of myocardium appears paler and dryer than normal. Sometimes, focal, blotchy, red-purple areas of hemorrhage are found. This is essentially the picture during the first forty-eight to seventy-two hours. At first the changes are very slight and difficult to make out, but they become progressively more distinct.

As soon as any degree of leucocytic infiltration has occurred, the infiltrated areas become yellow-brown in color. In an infarct about four days old a fine yellow line or border can be seen around its periphery. As the infiltration becomes more extensive this yellow band becomes broader in extent, and sometimes even a yellow-green in color. This is particularly true of infarcts six to eight days old.

The removal of muscle fibers shows itself in two ways. In the first place, a reddish-purple zone is found around the periphery of the infarct as the result of the formation of granulation tissue. The color is due to the presence of numerous newly-formed capillaries filled with erythrocytes. In the second place, the actual removal of fibers results in a shrinkage in the volume of the whole infarct. Therefore, the thickness of the myocardium in the infarcted area decreases, and a definite depression can be seen around the periphery of the infarct when it is viewed in cross section. This process first becomes apparent grossly after eight to ten days.

Continued healing results in an increase in the width of this band of depressed granulation tissue. The central mass of necrotic muscle gradually decreases in amount and assumes a pale, red-brown color. At three to four weeks, usually only small islands of necrotic muscle are found, and these are completely surrounded by granulation tissue.

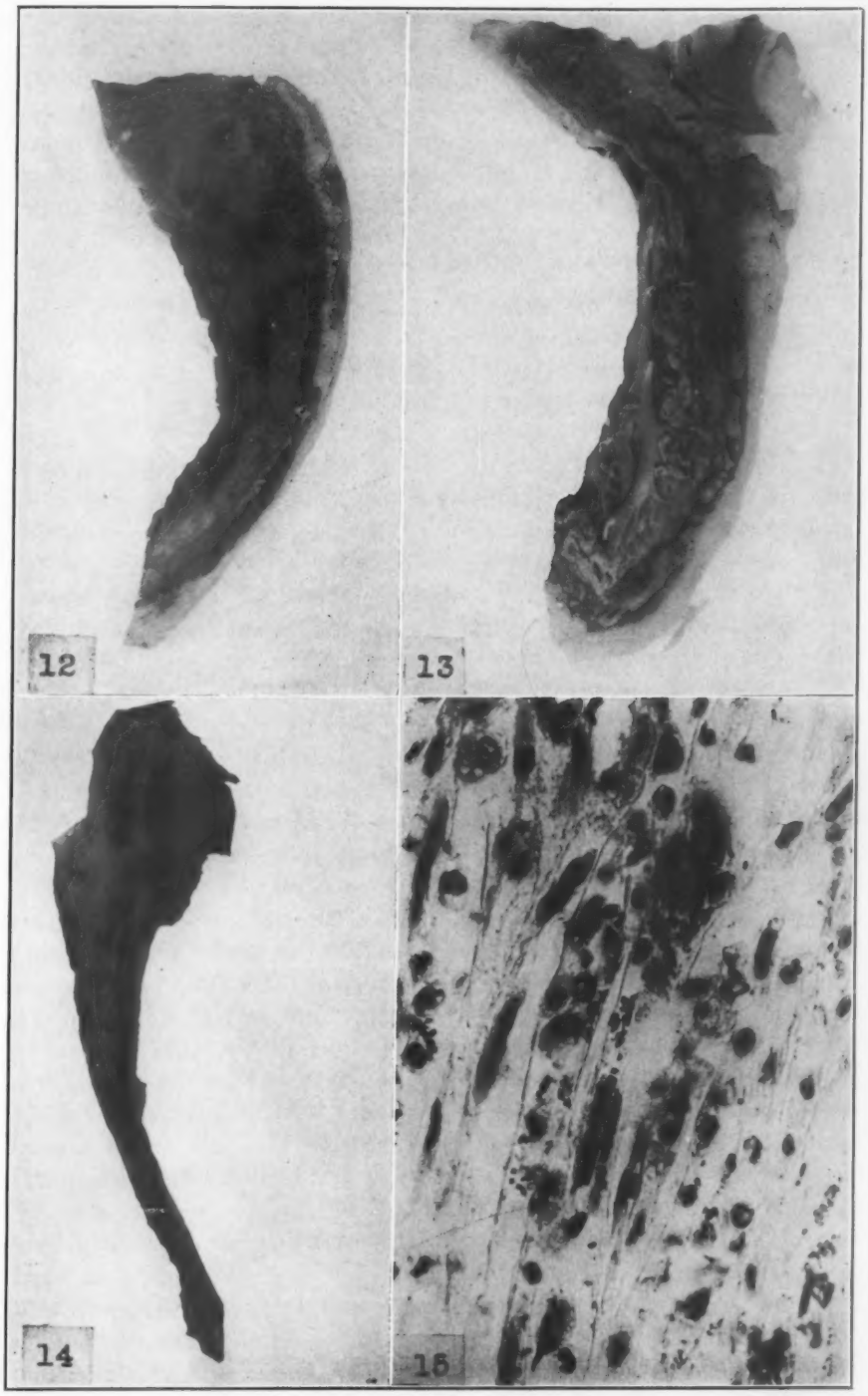
As this granulation tissue becomes older its collagen content increases, and the capillaries are compressed and less prominent. As a result of this, it becomes much paler and appears somewhat gelatinous. As the infarct becomes older it contracts more and more and eventually is transformed into a shrunken, firm, white, fibrous scar. It presents this appearance after about two to three months, and grossly no further change can be seen to take place.

Fig. 12.—Gross photograph, seven-day infarct. Longitudinal section of wall of left ventricle. Epicardial fat is shown along right border. Infarcted muscle stands out as irregular pale areas, in contrast to normal, darker, uninfarcted muscle. There is a fresh thrombus on the endocardial surface.

Fig. 13.—Gross photograph, fourteen-day infarct. Longitudinal section of wall of left ventricle with epicardial fat along right border. The unremoved infarcted muscle can be seen as pale islands, surrounded by a dark, depressed zone of granulation tissue. Here peripheral muscle fibers have been removed and replaced by blood vessels and connective tissue. The myocardial wall is somewhat decreased in thickness.

Fig. 14.—Gross photograph, infarct 6, or more, months of age. Longitudinal section of wall of left ventricle. Epicardial fat may be seen to left. The myocardial wall is very shrunken and consists of pale scar tissue. Necrotic muscle is completely removed.

Fig. 15.—Photomicrograph, high power, ten-day infarct. Detail, to show method of removal of necrotic muscle. Fibers fragmented but have not lost cross striations. Fragments are surrounded by histiocytes which seem to dissolve and phagocytose them. Polymorphonuclear leucocytes are rare at this stage.



Figs. 12 to 15. *(See opposite page for legends.)*

Similar changes occur in the pericardium and endocardium. The early fibrinous pericarditis can be seen as a thin, nonglistening, and easily detached layer of fibrin. As this becomes organized it adheres firmly to the epicardium and is eventually transformed into a focal, white area of fibrosis. In the same way the endocardial thrombus becomes more adherent and is gradually transformed into a thickened plaque of connective tissue which is eventually covered by endothelium.

FURTHER COMMENTS

Discrepancies.—In this group of infarcts a certain number were found which seemed too young or too well healed for their supposed age. A few of these discrepancies were almost too great to be explained at all, but the less marked ones can be accounted for by one or both of the following factors.

1. The size and the location of the infarct have an influence on the rate of healing. Small infarcts heal more rapidly than large ones. Subendocardial infarcts heal less rapidly than those in the center of the myocardium or beneath the epicardium.

2. The rate of healing also seems dependent upon the competency of the remaining circulation. If the coronary vessels show a marked degree of diffuse arteriosclerosis, with narrowing of their lumina, the rate of healing will be slower than it would if the remaining vessels were essentially normal. In the same way, if the circulation in the myocardium is somewhat inadequate as a result of a failing heart or generalized anemia, healing probably will not be so rapid and efficient as when adequate collateral coronary circulation is present.

In the cases in which there were greater discrepancies, we can only assume either that the history was inaccurate, or that two or more infarcts were present in the heart and that the microscopic sections were taken only from the one which had caused no definite symptoms.

Comparison of Healing of Experimental and Human Infarcts.—The process of healing of myocardial infarcts in man is very similar to that of the experimental lesions in the dog's heart, as described by Karsner and Dwyer.[9] Hemorrhage seems to be somewhat more prominent in the experimental lesions, and the only pigment found in them is hemosiderin. This is explainable on the ground that one would expect little or no waste pigment to be present in the heart of a young and healthy dog. A foreign-body giant cell reaction around necrotic muscle fibers is present in the experimental infarcts. This is rarely, if ever, seen in the human lesion.

Outside of these rather minor features, the chief difference is in the rate of healing of the infarcts. On the whole, the experimental lesions heal more rapidly than those seen in man. Signs of blood-vessel and connective-tissue proliferation are found at the end of forty-eight hours in the dog and not until ninety-six hours in man.

After eighteen days the experimental lesions are fairly well contracted and fibrosed, although remnants of necrotic muscle are still found at a much later date. In the human infarcts considerable necrotic muscle is still likely to be present after three weeks, and collagen, although present in some degree, is not as yet a very prominent feature.

The rate of healing of the experimental lesions is very similar to that in man when the human infarcts are small and the remaining myocardial circulation is in good condition. That human infarcts are likely to be larger is obvious when one considers that the wall of the left ventricle of a dog rarely measures over 6 mm. in thickness, whereas in human hearts, particularly the hypertrophied ones from patients who had had hypertension, the left ventricular wall is from 1.5 to 2 cm. thick. Also, the remaining intact coronary circulation is much more likely to be wholly normal in the dog. These two factors probably explain the difference in the speed of healing.

One feature which is observed both in the experimental and in the human lesions may have some clinical significance. This has already been mentioned; it is the fact that there is always a thin layer of surviving myocardium along the endocardial surface, extending into the myocardium along the Thebesian veins. As this is less than half a millimeter in thickness, it probably plays no significant role in preventing rupture, but when one remembers that many of the finer branches of the conduction system lie in this region it does perhaps explain why cardiac arrhythmias are comparatively rare in cases of myocardial infarction.

This observation is also of interest when considered in relation to the formation of intracardiac thrombi on the endothelium over the infarcted area. Even when well-formed thrombi are beginning to undergo organization, a thin layer of surviving myocardium can usually be found lying between the thrombus and the infarcted myocardium. Although one cannot make out a definite layer of endothelial cells beneath such thrombi, it would seem logical to believe that its disappearance was more likely to be the result of the thrombus formation than the cause of it. It does not seem probable that specialized cells such as cardiac muscle fibers should survive ischemia, while unspecialized endothelial cells should not. Also, along the Thebesian veins, where a thin layer is also spared, but where thrombus formation rarely occurs, both muscle and endothelium survive. Therefore, it would seem more logical to interpret the thrombus as a result of local dilatation of the heart plus stagnation of the blood in this area, than as a reaction to the necrosis of the endothelium.

Cardiac Rupture.—The problem of the time of rupture of an infarcted myocardium is important. From a theoretical standpoint, sev-

eral factors seem to be of significance. Necrotic tissue is undoubtedly less resistant than viable tissue. Therefore, rupture would be expected to occur when necrotic tissue is most abundant and before any degree of replacement by connective tissue and blood vessels has occurred. Histologically, necrotic tissue is most prominent from the second to the sixth day. The influence of polymorphonuclear leucocytic infiltration is difficult to judge. It may tend to reduce the resistance of the necrotic tissue by enzymatic digestion of portions of it. If it does produce such an effect, it would reach its maximum between the fourth and sixth days.

Another factor of importance in this connection is the intraventricular pressure. The higher this pressure, the more likely rupture is to occur. When the valves are normal, the intraventricular pressure is dependent on the pressure in the peripheral circulation; valvular abnormalities, particularly aortic stenosis, will, per se, cause it to be high. A preceding hypertension is common. It was present in more than one-third of the cases reported by Levine.[3] The same author states that a drop in blood pressure usually occurs at the time that infarction takes place, or soon thereafter, and that the blood pressure does not usually return to as high a level as before, but that in some instances the blood pressure may rise again a few days after the infarction.

In our eight cases of cardiac rupture the blood pressures after infarction were as follows: 173/90, 150/100, 140/80, 130/90, 110/78, 110/70, 90/70, 90/50. It is interesting to note that the only case in this group in which aortic stenosis was associated with infarction and rupture was the last.

After consideration of all of these more or less theoretical aspects, the optimum time for rupture to occur seems to be some time within the first ten days after myocardial infarction.

In our series, the ages of the infarcts at the time of rupture were the following:

1 day	1
2 days	1
3 days	1
6 days	2
7 days	1
9 days	1
12 days	1

The group is, of course, too small to allow extensive conclusions. From Levine's monograph one can take eight or nine additional cases. In his series of forty-seven autopsy cases, rupture occurred in nine. Calculating the age of the infarcts from the histories given, the following data are obtained:

1 day	1
3 days	1
4 days	1
6 days	2
11 days	1
14 days	2
5 weeks	1

Combining these two groups, a series of seventeen ruptured hearts is obtained, with the following distribution:

1 day	2
2 days	1
3 days	2
4 days	1
6 days	4
7 days	1
9 days	1
11 days	1
12 days	1
14 days	2
5 weeks	1

In the combined series, eleven, or 65 per cent, occurred in the first week, and five, or 29 per cent, in the second week.

A group of thirty-four cases of rupture of the heart following myocardial infarction was reported by Benson, Hunter, and Manlove.[10] They did not give sufficient data to enable one to estimate the actual age of the infarcts in their series, but twenty-nine are described as acute infarcts and four as acute infarcts superimposed on old ones; in one case there was dissecting rupture of an aneurysmal dilatation, following infarction which occurred about three months before death.

Combining these figures, it is justifiable to conclude that if a heart is going to rupture after infarction, it is most likely to do so during the first week; it may rupture during the second week; but rupture after the third week is rare, and when it does happen it is usually the result of some complicating factor, such as a fresh infarct.

CLINICAL APPLICATION

Of the greatest importance, of course, is the clinical application of the information that has come from this study of the speed of healing of myocardial infarction. We can now rest assured that in most cases repair proceeds steadily and in a fashion similar to that of scar formation in other parts of the body. In a month's time there is almost complete healing of small infarcts. Large infarcts require a few weeks longer, up to two months, to heal completely. There are rare

instances in which islands of unorganized necrotic muscle may remain longer, more or less as foreign bodies in the midst of myocardial scars; it is not likely that such unresolved lesions play much of a role, since they are surrounded by the thick, strong, fibrous tissue of the scar.

The two points of difference between the healing of a myocardial infarct caused by coronary disease and a traumatic lesion of muscle or bone elsewhere in the body are (1) that the myocardium must continue to function during the process of repair, whereas bone, skeletal muscle, or ligaments are immobilized, and (2) that the blood supply available for the healing of the cardiac lesion may be limited because of widespread narrowing of the coronary arteries. Thus, although it is well known that a small infarct may heal completely and cause little or no abnormality of cardiac size, function, or reserve, despite the lack of all treatment, nevertheless, there is no question that the strain of increased heart work, or even the work of the heart at rest, in some cases, may be too great when the myocardial infarct is large, with resulting cardiac dilatation and even failure. The second point is probably not so significant, for apparently a rich blood supply is not needed to promote good healing; even in the grave cases of our series, in which the patient died relatively early as the result usually of the heart disease itself, and had extensive coronary sclerosis, the healing of the infarct was in active swing from the very beginning.

Thus, our findings support the more or less empirical custom of those who advise for patients with small- to moderate-sized myocardial infarcts, without complications, one month of rest in bed (the first two weeks absolutely complete), and one month of very carefully graded convalescence, with a third month to consolidate recovery and to re-establish good health both of body and mind. To advise less than three weeks in bed is unwise, even for patients with the smallest myocardial infarcts, provided we are sure of the diagnosis; and it is almost equally unwise to advise prolonged bed rest in the absence of complications or when the infarct is not very large, because of the needlessness of so doing and the harm to the patient's health in general and to the morale and happiness of himself and of his family.

SUMMARY AND CONCLUSIONS

Seventy-two autopsy cases of myocardial infarction, in which the age of the infarct could be accurately determined, were studied in order to ascertain the speed of healing of the infarcts.

The characteristic gross and microscopic features of infarcts of various ages are described. Necrosis of muscle and infiltration by polymorphonuclear leucocytes are the important features of the first week. Removal of the necrotic muscle and replacement by connective tissue predominate during the next five weeks. Beginning at about the second week, the newly formed connective tissue lays down in-

creasing amounts of collagen. This collagen gradually increases in amount and becomes more dense. This process reaches a maximum at about three months, and thereafter very little change takes place.

Grossly, evidence of the removal of muscle fibers and their replacement by connective tissue and blood vessels can be seen in the form of a zone of red, depressed tissue surrounding pale brown areas of necrotic muscle. As healing proceeds this increases in extent, while the amount of necrotic muscle decreases. The increase in collagen causes the granulation tissue to become paler and gradually transforms it into a pale, firm, fibrous scar.

The process of healing of human infarcts in our series was compared with that of experimental infarcts produced by other investigators.

The following are the conclusions resulting from this study:

1. The age of an infarct can be judged fairly accurately from the histologic picture during the first three weeks. After this the estimation is not very accurate.

2. The speed of healing is in part dependent upon the size and position of the infarct and in part upon the state of the remaining myocardial circulation.

3. Small infarcts are almost completely healed after five weeks. Large infarcts are completely healed, or undergo no further discernible change, after two months.

4. Rupture of the heart is most common during the first week, may occur during the second week, but is rare thereafter. Histologically, much of the necrotic muscle has been replaced by connective tissue by the end of the first fortnight.

5. The healing of infarcts in human hearts is similar in most respects to that of experimental lesions in animals, except that the process is slower.

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COMBINED SYPHILITIC AORTITIS AND RHEUMATIC DISEASE OF THE HEART

Report of Four Cases

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ALTHOUGH the combination of rheumatic disease of the heart with syphilis of the aorta is not extremely rare, an analysis of the available literature up to the present time discloses less than thirty case reports. A study of these cases indicates that approximately fourteen are quite definitely authenticated by both gross and microscopic observations. These include those reported by Sager and Sohval, Cabot, and Lisa and Chandlee. The genuineness of the remaining cases is open to question because no microscopic observations were reported. There are five cases in unavailable foreign literature which should be included in this group. Sager and Sohval,[1] reviewing the literature up to 1934, found seven reported cases of combined syphilitic and rheumatic disease of the heart and aorta. They presented three cases of their own, in which syphilitic aortitis was associated with both syphilitic and rheumatic infection of the aortic valve. These are the only ones in which this particular combination was present. In Cabot's[2] series of five cases, syphilitic aortitis was associated with rheumatic endocarditis of the various valves. Lisa and Chandlee[3] reported six cases of syphilitic aortitis combined with rheumatic disease of either the myocardium or endocardium. In one of these, the syphilitic process involved the aortic valve.

The cases of Dumas and Brunat and Gallavardin and Gravier belong among those in which this combination has been less conclusively demonstrated. In Dumas and Brunat's[4] case, syphilitic aortitis was associated with mitral stenosis and a chronic, cicatricial endocarditis. Although marked stenosis of the mitral valve was present, the lesions both in the aorta and mitral valve were considered to be syphilitic. Gallavardin and Gravier[5] reported four cases in which syphilis of the aorta was combined with various rheumatic valvular lesions. In two cases, syphilitic aortitis was associated with rheumatic disease of two or more valves, while in the other two the syphilitic process was combined with rheumatic aortic stenosis. The microscopic findings were not reported in these cases.

Because of the relative frequency of syphilitic heart disease in this locality, an attempt was made to ascertain the incidence of this com-

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bination of diseases by a study of the autopsy material of the Vanderbilt Hospital. From 1925 to 1937, 1,841 autopsies were performed, and cardiovascular syphilis of all types was found in fifty-seven instances. There were also thirty-five cases of active rheumatic heart disease and thirteen cases of inactive rheumatic heart disease. Among these, there were four instances of syphilitic aortitis associated with either rheumatic endocarditis or rheumatic myocarditis.

CASE REPORTS

CASE 1 (V. H., No. 74001).—The patient was a 44-year-old white woman, who gave no history of rheumatic fever, chorea, or syphilis. She was admitted to the hospital Feb. 13, 1937, with lobar pneumonia of five days' duration. The past history revealed that she had first experienced exertional dyspnea fourteen years before admission, and that this was frequently associated with attacks of knifelike precordial pain which showed no tendency to radiate. In the preceding five years she had had dependent edema on several occasions. During the latter period, these symptoms had been fairly easily controlled with digitalis, and she had been able to go through a full-term, normal pregnancy without aggravation of her condition. However, nocturnal dyspnea had been present for two months prior to admission.

On admission, she displayed cyanosis of the lips and nail beds, with labored breathing, a cough which was productive of bloodtinged sputum, and a temperature of 102.2° F. There were evidences of consolidation of the right middle and lower lobes. The point of maximum intensity of the cardiac impulse was 9 cm. from the midsternal line in the fifth intercostal space. The right border of the heart was 3 cm. to the right of the midsternal line in the fifth intercostal space, and the retromanubrial dullness measured 7 cm. in width. A rough, loud, systolic murmur was heard over the entire precordium, but with maximal intensity over the aortic area; it was transmitted over the neck vessels only moderately well. In the aortic region the murmur was loud, rough, and rumbling. The aortic second sound was absent, and there were no presystolic or diastolic murmurs. The pulse was small in volume and not well sustained. The blood pressure was 128/86 in both arms, and slightly higher in the legs. The lower border of the liver was felt one centimeter below the costal margin in the midclavicular line. There was no ascites, and the lower extremities were not edematous. The erythrocyte count on admission was 5.02 million, with 11.5 grams of hemoglobin. The leucocyte count was 21,950, 95 per cent of which were neutrophils. The urine showed nothing of note, and blood cultures were repeatedly sterile. The blood Wassermann reaction was strongly positive. Sputum cultures were positive for the type IV pneumococcus. A roentgenogram of the chest showed marked right auricular enlargement, a very prominent aorta, and complete consolidation of the upper lobe of the right lung. The patient grew worse progressively, and expired seven days after admission. Clinical diagnoses: (1) lobar pneumonia, upper lobe of right lung, due to type IV pneumococcus, (2) aneurysm of the ascending aorta, (3) rheumatic aortic stenosis, and (4) syphilis of the aorta.

Autopsy.—The heart weighed 300 grams. As it lay in situ, there was marked displacement of the right border caused by a tremendous dilatation of the first portion of the aorta. This was entirely to the right and slightly downward, so that it partially overlay the right auricle. The epicardium was not remarkable, there were no mural thrombi, and the chambers of the heart were not dilated. Myocardial scarring was absent, but the wall of the left ventricle measured 22 mm. in thickness, being slightly hypertrophied. The tricuspid and pulmonic valves appeared normal in all respects, and, aside from a slight fibrous thickening of the leaflets, the mitral

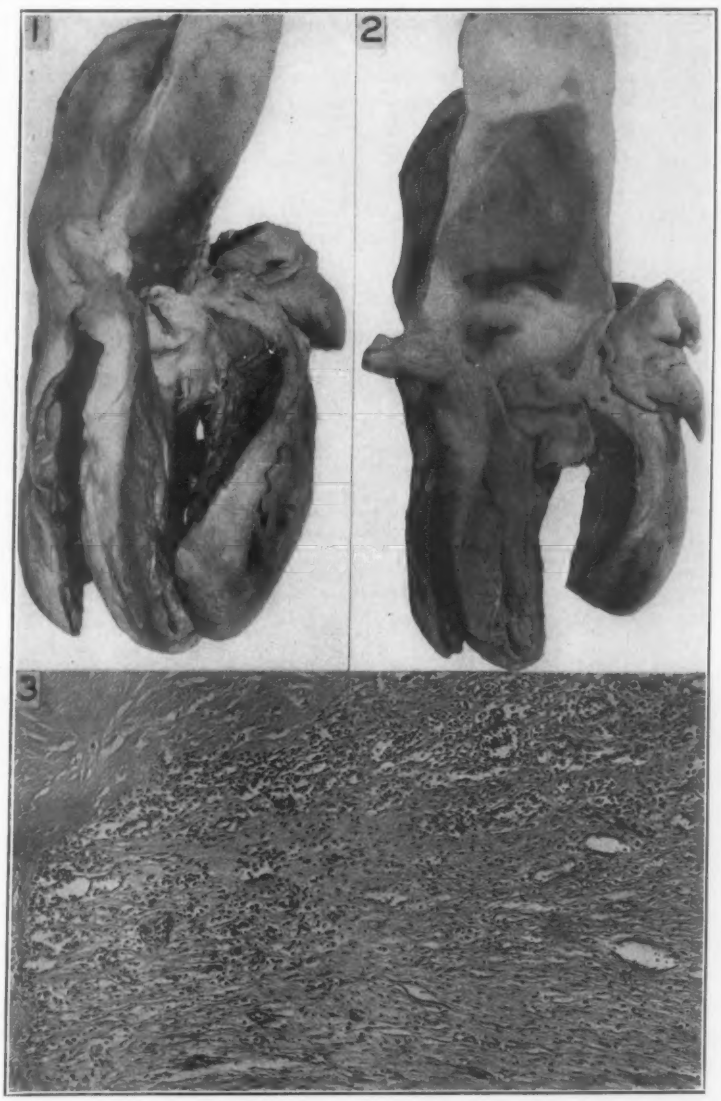
valve showed nothing remarkable. On section, the aortic ring was extremely firm. The cusps were distorted and fused into a solid, thick, projecting, shelflike structure, in the center of which was a narrow, "fish-mouthed" lumen. The attachments of the cusps were recognizable from the upper surface, and shallow sinuses were still present from which the coronary arteries arose as usual. The aortic ring measured 7 cm. in circumference, and the "fish-mouthed" lumen was 1½ cm. in length by 3 mm. in width. The shelflike cusps were 4 to 5 mm. in thickness. On the undersurface were several minute, irregular depressions, and when a small probe was passed through the largest of these it emerged on the upper surface in a small nodule of fibrous tissue. Immediately beyond the aortic valve the aorta expanded abruptly into a large, fusiform, aneurysmal dilatation, measuring 6 by 8 cm. At the origin of the left carotid artery the aneurysm abruptly ceased, and a low, ridgelike projection marked its termination. There was no stenosis at this point. Within the aneurysm, the aortic wall was thin, irregular, and less elastic than elsewhere. There were fine longitudinal wrinkles just beyond the aortic valve.

Microscopically, the left ventricular muscle was hypertrophied, and there was a diffuse interstitial fibrosis which was largely perivascular. In rare instances there were perivascular groups of large and dark-staining cells which were suggestive, but not typical, of Aschoff bodies. The small arteries showed a moderate intimal fibrosis. A section through the aortic valve showed a diffuse, atrophic, and partially calcified fibrous thickening which had undergone hyalinization. Along the inner border, adjacent to the endocardium, there were innumerable fibroblasts and small round cells, as well as many thin-walled capillaries. This portion showed organization. Along the outer border of the leaflet, organization had occurred in the past, but coagulation necrosis was present. There were no areas of acute ulceration or vegetation, and the perivascular round-cell infiltration characteristic of a syphilitic process was absent. A section of the aorta through the ridge marking the termination of the aneurysm showed a fairly thick fibrous tissue proliferation which was partially hyalinized. The internal lamina was unusually thick and conspicuous, and the media appeared loose. There was some distortion of the elastic laminae, and a few small scars were present in the outer portion. The vasa vasorum showed little sclerosis, but the vessels along the junction of the adventitia and media were surrounded by round cells and plasma cells. Similar pictures were found elsewhere in the aorta. The anatomical diagnoses were: (1) Lobar pneumonia, right upper lobe, with extension to the right middle and lower lobes, (2) syphilitic aortitis with fusiform aneurysm of the arch and ascending aorta, (3) rheumatic aortic stenosis, inactive, with left ventricular hypertrophy, (4) acute fibrinopurulent pleurisy, and (5) parenchymatous degeneration of the liver and kidneys.

CASE 2 (V. H., No. 3155).—This patient, a 43-year-old negro, was admitted to the hospital Nov. 4, 1933, with acute pulmonary edema of one day's duration. He had had exertional dyspnea for two years, but had not been incapacitated. Edema of the lower extremities had been present occasionally, but this was apparently due to old varicosities and trophic ulcers of the feet. No history of rheumatic fever was obtained, but the patient had had a painless penile lesion twenty-six years before admission, for which he had received no treatment. In 1927, bilateral femoral sympathectomy was done in an attempt to heal the trophic ulcers of the feet. At that time, the blood and spinal fluid Wassermann reactions were strongly positive. His blood pressure at that time was 168/97, but there was no cardiac enlargement.

Physical examination revealed an acutely ill negro who was sitting propped up in bed; his breathing was difficult and labored, and he had a brassy cough which was productive of slightly bloodtinged sputum. There was edema of the lower extremities. The voice was hoarse and high-pitched. The cervical veins were distended even in the upright position, and did not collapse on inspiration. The retinal arteries

were tortuous, but there were no retinal hemorrhages or exudate. A tracheal tug was demonstrable. The pupils were unequal, irregular, and reacted sluggishly to light. Acute pulmonary edema was present. The point of maximum intensity of the apex beat was 14 cm. from the midsternal line in the sixth intercostal space. There were no shocks or thrills; the rhythm was normal and there were no diastolic murmurs. A short systolic murmur was heard over the aortic area and the pulmonic second sound was louder than the aortic second. The liver was not palpably enlarged, but ascites was present. A roentgenogram of the chest showed a large mass in the



Figs. 1 and 2, Case 1.—The heart and aorta, illustrating the aneurysm of the ascending aorta, and the marked thickening, distortion, and contraction of the aortic cusps.

Fig. 3, Case 1.—Photomicrograph of aortic valve. The diffuse scarring, with hyalinization and organization, is apparent. In the upper portion, a rather marked round-cell infiltration is seen.

upper mediastinum suggesting an aneurysm involving the innominate artery and aortic arch, with marked prominence of the aortic knuckle and dilatation of the descending aorta. Roentgenologically, the heart was enlarged to the left. Routine laboratory examinations, other than the roentgenogram and including the blood Wassermann reaction, showed nothing remarkable. The patient grew worse rapidly, and died Nov. 7, 1933, three days after admission. Clinical diagnoses: (1) Syphilitic aortitis with aneurysm of the arch of the aorta, (2) cardiac hypertrophy, dilatation, and insufficiency, (3) bronchopneumonia.

Autopsy.—The heart weighed 370 grams and was enlarged to the left. The epicardium was not remarkable. The myocardium was streaked with fat, and there were several small areas of scarring. The left ventricular wall was 1.5 cm. thick; the auricular wall was of normal thickness. The endocardium was smooth and glistening, but showed a few small, white scars. The tricuspid valve showed thickening and rolling of the edges of the valve leaflets, with a ballooning of the central portion. The chordae tendineae were prominently shortened and thickened. The pulmonic valve appeared normal grossly. The mitral valve was thickened and the edges rolled, so that some of the chordae tendineae, which were shortened and thickened, were attached to the upper surface of the valve leaflets. The aortic cusps sagged somewhat; there were thickening and scarring along the line of the attachment, and the commissures were markedly widened. The sinus of Valsalva was widely opened at the orifices of the coronary arteries, but the latter appeared normal grossly. There were small atheromatous plaques at the root of the aorta, but, as the arch was approached, there was an irregular wrinkling of the intimal surface with irregular plaques. Between the origin of the great vessels of the neck and the subclavian artery there was a large sacculated aneurysm containing laminated thrombi. The aneurysm extended upward into the neck and was intimately in contact with the trachea. The aorta was somewhat curved into the left pleural cavity below the aneurysm.

Microscopically, the epicardium appeared normal, while the myocardium exhibited edema and scarring of moderate degree. The myocardial fibers were hypertrophied, and brown atrophy of many of the fibers was present. Here and there were condensations of connective tissue suggestive of Aschoff bodies, but no typical cells were seen. The endocardium was edematous, and at one point there was a raised, fibrinous bundle in which blood cells and mononuclear cells were found. The coronary arteries showed intimal thickening of moderate degree. There was an irregularity in both the intima and media of the aorta caused by replacement of normal structures by fibrous tissue which in many instances was hyalinized. Scattered throughout the fibrous tissue were collections of fat, cholesterol crystals, and small collections of calcium. The scarring of the media almost replaced the normal structures. The vasa vasorum were thickened, and there was a perivascular infiltration of round cells and plasma cells which was very prominent. Anatomical diagnoses: (1) Syphilitic aortitis with aortic insufficiency and aneurysm of the arch of the aorta, (2) cardiac hypertrophy, dilatation, and insufficiency, (3) rheumatic mitral and tricuspid valvulitis, inactive, (4) acute passive congestion of the lungs and liver, (6) carcinoid of the cecum with metastasis to the liver, (7) thrombosis of the middle cerebral artery, and (8) perforating ulcers of the feet.

Case 3 (V. H., No. 67804).—The patient, a 39-year-old negro, was first admitted to the hospital Nov. 24, 1934. He had been well until two years prior to admission, at which time he developed exertional dyspnea which had been progressive. Two months before entering the hospital he developed nocturnal dyspnea, and had to spend most of the time sitting upright in a chair. It was not until three days prior to admission that edema of the ankles appeared, and, with it, abdominal swelling became apparent. In addition, he had had periods of oliguria, alternating with nocturia and polyuria, for two months. He had had a gonorrheal infection at the age

of 24, which was followed in two months by a chancre. He received no treatment for syphilis at that time. The patient also gave a history of repeated attacks of sore throat which were frequently accompanied by pains in the knees and hips. These attacks became apparent after the age of 25. There was no other history suggestive of rheumatic infection. Ten years before admission to the hospital he was found to have a positive blood Wassermann reaction, and received an indefinite number of intravenous injections, after which his Wassermann reaction is supposed to have been negative.

Physical examination revealed a well-developed negro who exhibited extreme orthopnea, edema of the sacrum and lower extremities, and ascites. There was a marked carotid and substernal pulsation, the pulse was of the water-hammer type, and the blood pressure was 160/50 in both arms. The cardiac impulse was thrusting and heaving in the sixth intercostal space in the anterior axillary line. Suprasternal dullness was increased to the right, and the right border of the heart was 3 cm. beyond the midsternal line. At the apex there were a faint, systolic murmur, a diastolic murmur, and a rough presystolic rumble. As the left sternal border was approached the systolic murmur was still heard and the diastolic murmur became louder, reaching its maximum intensity in the fourth intercostal space on the left, at which point it had a musical, cooing-dove quality. The aortic second sound was replaced by this murmur. There was no tracheal tug, the pupils were equal, and the temperature of the face was the same on both sides. The pulses were synchronous. Scattered moist râles were heard at the bases of both lungs. The lower border of the liver could be percussed but not palpated. An old penile scar was present, together with hard, satellite, regional lymph nodes. The deep reflexes appeared normal. Laboratory examination revealed a normal blood cell count, an occasional erythrocyte in the urine, and a 40 per cent excretion of phenolsulphonephthalein in two hours. The blood Wassermann reaction was positive, as was the Kahn. An electrocardiogram showed left axis deviation. The spinal fluid Wassermann reaction was negative. A roentgenogram of the chest revealed marked cardiac enlargement, particularly of the left ventricle.

The patient was digitalized, fluids were restricted, and he was given diuretics. He improved and was discharged Dec. 8, 1934. Following his discharge he was able to carry on his normal activities with some restriction of his mode of living, and had no recurrence of nocturnal dyspnea until May 1, 1935, at which time he again developed acute pulmonary edema. The findings at this time were as before, but he did not respond to therapy, and expired May 3, 1935. Clinical diagnoses: (1) Syphilitic aortitis with aortic insufficiency, and (2) cardiac hypertrophy, dilatation, and insufficiency.

Autopsy.—The heart weighed 700 grams and was enlarged in all diameters, particularly to the left, and the left ventricle was hypertrophied. The myocardium showed an occasional small scar. Small, mural thrombi were present in the auricular appendages, but the endocardium appeared otherwise normal. The mitral, tricuspid, and pulmonary valves were thin, delicate, and competent, and measured 10 cm., 13 cm., and 7.5 cm. in circumference, respectively. The leaflets of the aortic valve were rolled, the edges were thickened, and there was a wide separation of the commissures. The edges of the thickened and shortened leaflets were irregular and projected upward to an apex in their middle, giving the appearance of a triangle, the base of which was at the attachment of the cusps to the aorta. The aortic ring was not appreciably dilated, but the contraction, separation, and distortion of the leaflets made an unquestionable insufficiency. The left auricle was hypertrophied, elongated, and slightly dilated. The right ventricle showed similar changes. There were wrinkling and puckering of the first portion of the ascending aorta and arch. Several raised, translucent, wrinkled plaques were present near the aortic ring; they ended rather abruptly just beyond the arch of the aorta, where the wrinkling and puckering were

most distinct. There was a slight aneurysmal dilatation of the arch of the aorta, without definite sacculation. The coronary arteries were patent throughout, showing only an occasional, small, sclerotic plaque, but the process in the aorta encroached somewhat upon the orifices.

Microscopically, the epicardium appeared normal, while the myocardium showed scarring and hypertrophy of the individual fibers. In the interstitial tissue of the left ventricle there were accumulations of cells with dark-staining nuclei and abundant purplish-pink cytoplasm. Some of these were multinucleated, and in a few places a giant cell was seen. There were plasma cells and round cells distributed about these large cells which were quite distinctive of Aschoff bodies. In the aorta, great accumulations of plasma cells and a few round cells were seen about the vessels in the adventitia and media. Many vessels had invaded the media, and there was scarring with a loss of elastic tissue and remarkable irregularity in all three layers of the aorta. The intima was thickened by fibrous tissue, and was separated from the media in some areas. Anatomical diagnoses: (1) Syphilitic aortitis with aortic insufficiency, (2) cardiac hypertrophy, dilatation, and insufficiency, (3) rheumatic myocarditis, acute, (4) acute intracapillary glomerular nephritis, (5) thrombosis of the right auricular appendages, (6) multiple infarcts of the lungs, (7) chronic passive congestion of viscera, and (8) aortic dilatation without aneurysm formation.

CASE 4 (V. H., No. 35936).—A 32-year-old negro was first seen Nov. 24, 1930, complaining of difficulty in hearing, tinnitus, vertigo, diplopia, and headache. These symptoms had been present for five months. In addition, he had noted exertional dyspnea for one year, accompanied by edema of the ankles. Under treatment by his local physician, the dyspnea and edema subsided. During the two months prior to his first admission he had experienced two attacks of unconsciousness without convulsions. Five years prior to the onset of his illness he had had a painless, penile lesion, associated with inguinal adenopathy. There was no history suggestive of rheumatic fever. The positive findings on the first admission were: general lymph node enlargement, hyperactive deep reflexes, normal air conduction as well as bone conduction, but definite diminution in auditory acuity for the spoken voice. The vision was 20/20, and there was no papilledema or optic atrophy. A soft, blowing, systolic murmur was audible at the apex, but there was no evidence of cardiac enlargement. The blood pressure was 126/88. The blood Wassermann reaction was positive, as was the spinal fluid Wassermann. The mastic reaction on the spinal fluid showed a curve of 5431000000. A diagnosis of central nervous system syphilis was made, and during the next two months he received six injections of bismuth and two injections of neoarsphenamine (0.3 gm.).

On June 30, 1931, he was admitted to the hospital in coma. During the two weeks prior to admission he had had two convulsions, and, on the morning of admission, nine more. Coma had been present for six hours. The only positive findings on that admission were: rapid and deep respiration, hot and moist skin, contracted and unresponsive pupils, normal fundi, many rhonchi throughout the lungs, absent deep reflexes, and a blood pressure of 186/86. The blood sugar content was recorded as 347 mg. per cent, and the carbon-dioxide combining power of the blood as 17 vol. per cent. The urine was normal, and the nonprotein nitrogen content of the blood was 30 mg. per cent. A lumbar puncture revealed bloody spinal fluid, with an initial pressure of 110 mm. of water. The patient expired two hours after admission. Clinical diagnoses: (1) Diabetes mellitus, with coma, (2) syphilis of the central nervous system, type undetermined, (3) cerebral hemorrhage, site undetermined.

Autopsy.—The heart weighed 360 grams and was slightly enlarged. The epicardium and myocardium appeared normal grossly. The aortic cusps were thickened, particularly at their points of attachment, and there was a moderate sagging of the

cusps, but the commissures were not widened. Along the line of closure of the mitral valve there were numerous, small, firm, raised, translucent, pinkish-gray nodules, varying in length up to 3 mm. These were firmly attached to the superior surface of the valve and could not be torn away without tearing the cusp. They were not friable and did not show ulceration or other features of an acute bacterial vegetation. There was no rolling of the margin of the mitral cusps, and the

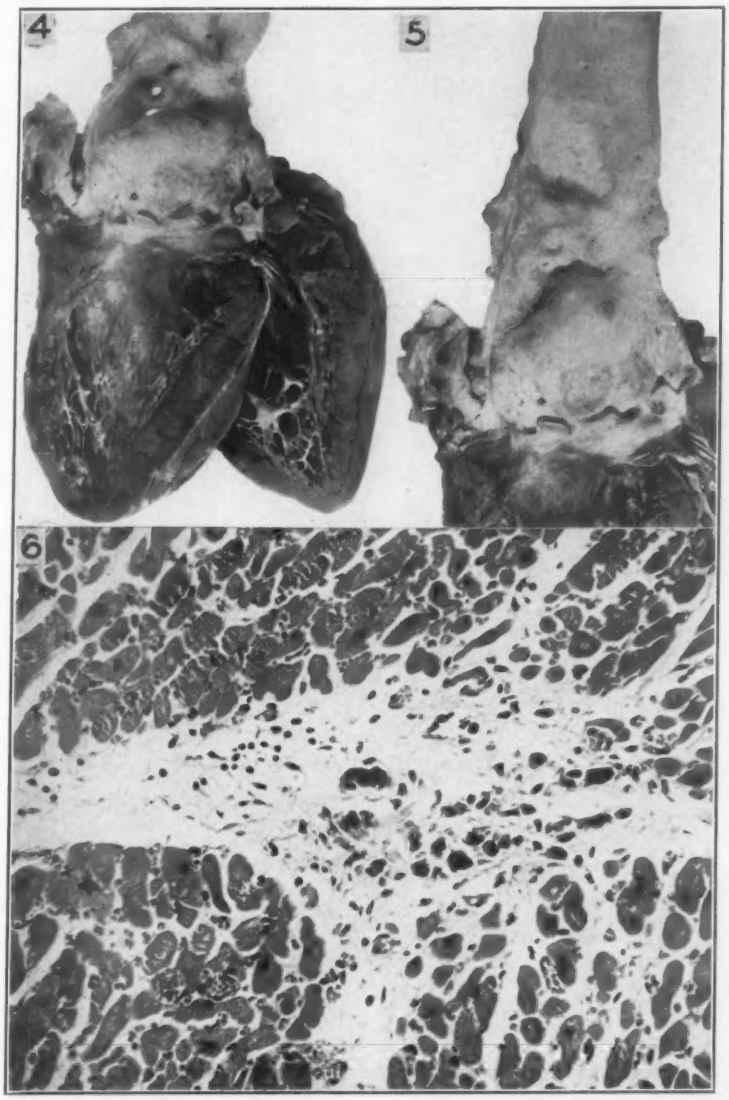


Fig. 4, Case 3.—Heart—hypertrophy and dilatation of left ventricle. The aortic cusps are rolled, thickened, and separated at their edges, and the commissures are widened. The first portion of the aorta shows well-defined wrinkled plaques.

Fig. 5, Case 3.—Aortic valve—classical aortic insufficiency, with syphilitic aortitis which stops rather abruptly just distal to the dilatation (beginning aneurysm) in the arch of the aorta. The syphilitic process encroaches upon the orifices of the coronaries to a slight degree.

Fig. 6, Case 3.—Photomicrograph of myocardium, showing a typical Aschoff body as observed in this case.

chordae tendineae were not abnormal. The remaining valves and endocardium appeared normal. The valve measurements were as follows: aortic, 7.5 cm.; pulmonic, 8 cm.; mitral, 9 cm.; tricuspid, 13 cm. At the base of the aorta there were numerous longitudinal wrinkles, as well as raised, yellowish plaques and pearly gray areas. The latter were the result of intimal thickenings, while the former were apparently associated with medial scarring. There was a slight dilatation of the posterior wall of the arch of the aorta. The lumina of most of the branches of the aorta were slightly constricted, and surrounded by radially arranged wrinkles. The intimal thickening increased toward the bifurcation, but the wrinkling disappeared in the upper portion of the thoracic aorta, ceasing very abruptly.

Microscopically, the epicardium appeared normal, but scattered throughout the myocardium were numerous small, fibrous scars. There were no areas of acute necrosis, but there were several areas of perivascular cellular infiltration. The predominant cell was relatively large, with clear, blue cytoplasm and a large vesicular nucleus. In these areas of cellular infiltration there were round cells and plasma cells in abundance, as well as an occasional polymorphonuclear leucocyte. These areas were typical Aschoff bodies. The intima of the aorta was thickened, and numerous slitlike spaces were seen within the intima. The media was the seat of profound changes characterized by numerous scars and many areas of perivascular round-cell infiltration. This same cellular infiltration was marked in the adventitia, and gave the characteristic picture of syphilitic involvement. Anatomical diagnoses: (1) Gumma of left frontal lobe, (2) syphilitic pachymeningitis and leptomeningitis, (3) syphilitic aortitis without aortic insufficiency, (4) syphilis of the aortic valve, and (5) rheumatic endocarditis, mitral valvulitis, and rheumatic myocarditis, acute.

DISCUSSION

The incidence of syphilitic aortitis, as determined by clinical and pathologic examination, has been variously estimated. Clawson and Bell,[6] in studying several hundred autopsies in Minnesota, found that syphilitic aortitis occurred in 2.6 per cent of the necropsies; White[7] has estimated that syphilitic aortitis represents not more than 4 per cent of all cardiovascular disease in New England. In a survey of 645 cases of organic heart disease in Tennessee, Laws[8] found that syphilis was the etiologic agent in 7.9 per cent of the patients, and that rheumatic heart disease was present in 10.5 per cent of the cases. From a study of the autopsy material of various localities, White found that rheumatic heart disease with mitral stenosis occurred in from 0.08 to 3.89 per cent of all necropsies. The lower figure represents the incidence in New Orleans, and the higher figure that at a New England hospital. Of 1,841 autopsies performed at the Vanderbilt Hospital, syphilitic aortitis, both symptomatic and asymptomatic, was found in 3 per cent, while rheumatic heart disease of all types and grades occurred in 2.6 per cent. In this group, rheumatic heart disease was present in 7 per cent of the cases of syphilitic aortitis, and syphilitic aortitis was demonstrated in 8 per cent of the cases of rheumatic heart disease. The incidence of this combination has been estimated by others. Cowan and Rennie,[9] in a clinical study of 104 patients with syphilis of the heart or aorta, found rheumatic involvement in 3.1 per cent of the cases. Reid,[10] in

studying seventy-eight autopsy cases of cardiovascular syphilis, found rheumatic heart disease definitely associated in two cases, and probably also in a third. White states that this combination occurs in less than one per cent of all cases of cardiovascular disease. That our figures are higher than those previously reported may be due to the fact that syphilitic aortitis occurs more frequently in this locality than in those in which the above cases were observed.

The more frequent occurrence of the combined lesions among the negroes in our group is probably of no particular consequence, for forty-one of the forty-seven patients with syphilitic aortitis were negroes. Twelve of the thirty-five patients showing rheumatic heart disease were negroes.

Various authors, in discussing the combined lesions, have suggested that one predisposed the heart to a subsequent infection by the other. Lisa and Chandlee thought that the syphilitic process might have rendered easier the secondary invasion by the rheumatic infection in those cases in which the rheumatic infection occurred after the syphilitic lesion. Warthin[11] believed that latent syphilis in a young person predisposed him to secondary bacterial endocarditis, and Coombs[12] also thought that a syphilitic valve was disposed to secondary infection. Friedlander[13] stressed the frequency of myocarditis in congenital syphilis, stating that syphilitic myocardial damage may often be the only manifestation of congenital syphilis. This is of interest, inasmuch as in two of our cases, in which the rheumatic infection almost certainly followed the syphilitic lesion, acute rheumatic myocarditis was present in association with syphilitic aortitis. According to Lisa and Chandlee, the syphilitic process may cause an exacerbation of a low-grade, asymptomatic, rheumatic heart disease of sufficient intensity to result in its passage into a clinical entity. However, there is, as yet, no definite evidence of any connection between the two diseases, and our series is too small to permit conclusions to be drawn.

In our series, the duration of congestive failure after the initial break in compensation varied from fourteen years to eighteen months. In Case 1, the patient lived fourteen years after the onset of exertional dyspnea; the rheumatic aortic stenosis was apparently the initial lesion and assumed the major role. The syphilitic aortitis and aneurysm of the aorta were secondary. The course in this case corresponded fairly closely with that of uncomplicated rheumatic aortic stenosis. However, in the three remaining cases, the duration of congestive failure averaged twenty-two months. This figure is much lower than the average usually encountered in pure rheumatic heart disease, and slightly higher than in cases of syphilitic heart disease. In this latter group the rheumatic lesions were of secondary interest and apparently remained silent, while the syphilitic process predominated and assumed its usual manifesta-

tions. The average duration of life after the onset of congestive failure was fourteen months in forty cases of syphilitic aortitis observed at the Vanderbilt Hospital.

Clinically, it is often impossible to establish the diagnosis of combined rheumatic heart disease and syphilitic aortitis. In three cases in this series this was true, and the diagnosis was made only at autopsy. However, in Case 1, the presence of aortic stenosis associated with clinical and roentgenologic evidence of aneurysm of the aorta and a positive blood Wassermann reaction made it possible to establish the correct diagnosis. This particular combination of the two lesions, and cases of aneurysm of the aorta with mitral stenosis and without aortic insufficiency are probably the only two combinations in which the diagnosis can be made with certainty clinically. One may suspect the coexistence of the two diseases in cases in which the following clinical features are present: (1) aneurysm of the aorta together with aortic insufficiency and a presystolic murmur, (2) mitral stenosis with aortic insufficiency in a case in which the presystolic murmur appeared prior to the diastolic murmur and in which there are clinical evidences of syphilis, and (3) aneurysm of the aorta with a diastolic murmur in a case in which there is a good history of previous rheumatic infection. There are undoubtedly other combinations which might be detected, but they are less certain than the above. In cases of obscure and bizarre cardiovascular disease in which there are a history of previous rheumatic fever and clinical evidences of syphilis, the possibility should be suspected and excluded. This is especially true if the course of the disease is much shorter than is ordinarily the case with uncomplicated rheumatic heart disease.

The difficulties encountered in making a diagnosis of the combined lesions is well illustrated by the following case. This patient, a 44-year-old white man, had acute, migrating polyarthritis in 1929, and sometime later was found to have a systolic murmur at the apex which had not been present at the first examination. In 1935, he contracted syphilis. In June, 1937, he developed exertional dyspnea which was rapidly progressive. One year later, examination revealed extreme cardiac hypertrophy and dilatation, an early systolic thrill limited to the aortic area, and a loud, high-pitched, rough, systolic murmur, followed by a softer diastolic murmur, in the second left intercostal space. As the apex was approached these murmurs were replaced by a loud systolic murmur, which, in turn, was followed by a late diastolic rumble. There was gallop rhythm at the apex. The blood pressure was 140/78, and the usual signs of cardiac insufficiency were present. The blood and spinal fluid Wassermann reactions were positive. This patient expired one year after the onset of congestive failure. At necropsy, he was found to have rheumatic endocarditis of the mitral and tricuspid valves with mitral stenosis and tricuspid insufficiency, healed bacterial endo-

carditis of the aortic valve which was superimposed upon what appeared to be a very early syphilitic aortitis with valvular involvement and also rheumatic valvulitis, and an inactive rheumatic myocarditis. The aortic valve was stenotic and insufficient, and a very extensive and destructive lesion was present. Two of the aortic cusps were perforated, and, grossly, the third resembled the typical syphilitic valve. Here, then, was a case in which there were both a history of rheumatic fever and syphilis with multiple cardiac signs and a very rapidly fatal termination. One observer believed that the patient had syphilitic aortitis with aortic insufficiency, while another made a diagnosis of rheumatic aortic and mitral stenosis with insufficiency. The possibility of combined syphilitic and rheumatic lesions was considered. This case is not listed with the other four in our series because, although the man probably had syphilis of the aortic valve in association with the rheumatic infection and the healed bacterial endocarditis, the nature of the pathologic changes was not indisputable.

SUMMARY

1. The clinical and pathologic findings in four cases of combined syphilitic aortitis and rheumatic heart disease are reported and discussed.

2. Contrary to the previously accepted idea that rheumatic heart disease occurs rarely in the southern states, our figures show that, clinically, rheumatic heart disease occurs more frequently in this locality than syphilitic aortitis, and almost as frequently at autopsy.

3. From the evidence now available, one can draw no conclusions concerning the possible interrelationship of these two forms of heart disease.

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THE EARLIEST CORRELATION OF CLINICAL AND EXPERIMENTAL AURICULAR FIBRILLATION

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FIBRILLARY activity of cardiac muscle was first demonstrated by Hoffa and Ludwig,[1] in 1850, as a result of their attempt to produce tetanic contractions in the ventricles of various cold-blooded animals and mammals by direct faradization. The same phenomenon was produced by Einbrodt,[2] in 1860, and later by Vulpian,[3] who also observed that a similar, but generally more transient, condition could be produced in the auricle of the dog. However, the clinical occurrence and importance of auricular fibrillation were overlooked for at least twenty-five years, and the condition was regarded primarily as a laboratory curiosity, being frequently produced by direct faradization of the heart and the administration of various toxic and pharmacologic agents. It is true that irregularities of the pulse in man were observed and recorded by Marey[4] as early as 1863, and later by Riegel,[5] Sommerbrodt,[6] Janowski,[7] and numerous other clinicians. These irregularities were given a variety of names, such as the "mitral pulse," delirium cordis, pulsus irregularis perpetuus, and the absolutely irregular pulse. However, they were neither adequately recognized as definite clinical entities, nor correlated with those experimentally observed in animals, such as auricular fibrillation. Indeed, it was not until 1903 that Hering[8] definitely established the fact that the absolutely irregular pulse is a definite clinical entity. With the introduction of the electrocardiograph, Lewis[9] and Rothberger and Winterberg[10] ultimately proved that the majority of these irregularities observed in man were one and the same, and were the clinical counterpart of the experimental auricular fibrillation observed in animals.

The correlation between the clinical and laboratory observations was suggested, however, prior to the publication of the papers of Lewis and Rothberger and Winterberg. This earlier correlation was an outgrowth of the investigations of Arthur Cushny, undertaken while he was professor of Materia Medica and Therapeutics in the Medical School of the University of Michigan, at Ann Arbor. Cushny[11] states that he had been interested in cardiac irregularities as early as 1890. He was familiar with auricular fibrillation as produced in animals, both by direct faradization of the heart and by the administration of various drugs, such as digitalis, and he had frequently observed the condition in his labora-

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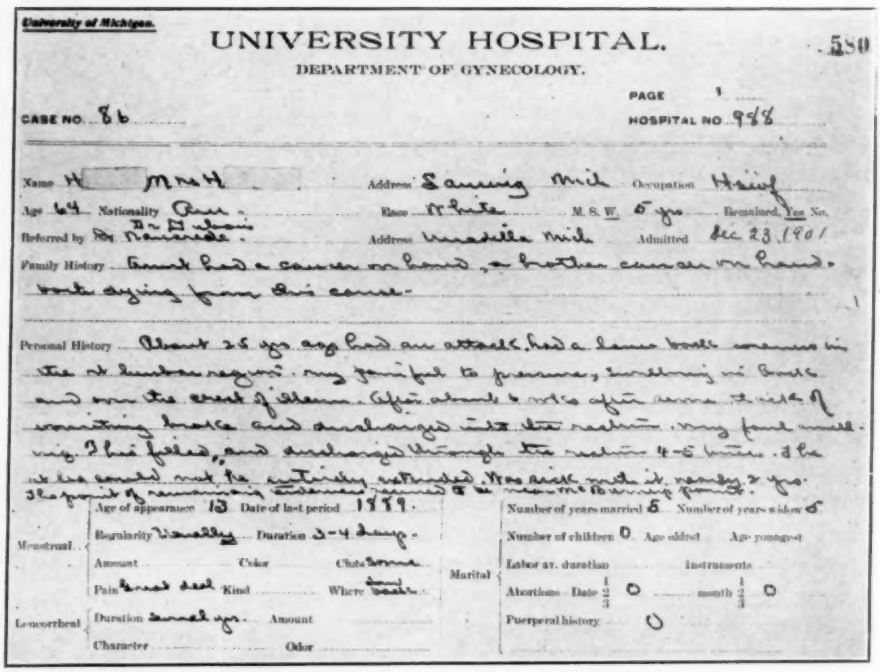
tory. This led him to wonder about the nature of the various pulse irregularities observed in man. In collaboration with George Dock, who was at that time professor of Medicine at Ann Arbor, he was able to study such irregularities in man by means of the Jacquet sphygmochronograph. With this instrument he recorded the radial pulse in patients with all of the types of irregularities of the heart which he had observed in his laboratory animals. In 1899 he published[11] the results of this work, and in this paper he pointed out the similarity of the clinical sphygmogram in cases of delirium cordis and that obtained from dogs during auricular fibrillation, and suggested that the two conditions might be identical. Previous to this, no writer had even faintly hinted at such an idea, but, nevertheless, the suggestion was entirely overlooked at the time.

In 1906, and again in 1907, Cushny,[12, 13] in collaboration with Edmunds, published and compared pulse tracings from a patient with delirium cordis and those from dogs with experimentally produced auricular fibrillation. With these more complete data, the suggestion regarding the identity of the two conditions was reiterated. This suggestion was first recognized and discussed by Wenckebach,[14] later by Lewis,[9] and more recently by Garrey.[15] In 1912, Lewis[16] pointed out that his remembrance of the original suggestion and paper by Cushny and Edmunds[12] finally led him to compare more closely, and finally to correlate, the electrocardiograms from animals with auricular fibrillation with those obtained from patients with an absolutely irregular pulse. In general, however, more recent writers (e.g., White[17]) appear only vaguely aware of this contribution, and have given it scant notice. Because this was the first correlation of the laboratory and clinical observations, because the existence of this correlation is not more generally known, and, finally, because there is an important and historically interesting phase of this story that is entirely unknown, a presentation of the complete history of this contribution seems justified.

On Dec. 23, 1901, Mrs. H. H., a 64-year-old widow, entered the University Hospital, in Ann Arbor, complaining chiefly of an ovarian fibroid. She was sent to the Gynecology Service of Dr. Reuben Peterson and was successfully operated upon. At this time Dr. Charles Edmunds was an intern on this service, and during his routine examination of the patient he observed a paroxysmal irregularity of the pulse. He had been interested in cardiac irregularities and had previously discussed with Cushny the latter's observation, made in 1899. This interest led him to make tracings of this patient's radial pulse by means of the Jacquet sphygmograph. The resemblance of these tracings to those he had seen Cushny make on dogs with auricular fibrillation aroused his curiosity, and he had Cushny examine the patient. The original hospital records of this patient, which are reproduced here in part (Figs. 1, 2, and 3), substantiate these statements. Fig. 3 is a portion of the daily

record of the patient, indicating the clinical observation of the paroxysmal irregularity of the pulse, and showing that the patient was examined by Cushny on Dec. 28, 1901, the day the pulse tracings were made. It is of interest to note the comment that the patient herself had noticed the irregularity previously. The pulse tracings that were made have been reproduced from the originals (Figs. 4 and 5). Cushny compared these tracings with those secured from dogs with auricular fibrillation (Fig. 6). He believed that the striking resemblance constituted excellent evidence in favor of his original suggestion.



University of Michigan.

UNIVERSITY HOSPITAL. 580

DEPARTMENT OF GYNECOLOGY.

CASE NO. 86 PAGE 1 HOSPITAL NO. 998

Name H. M. H. Address Saline Mich. Occupation Hsekp.

Age 64 Nationality Amer. Race White M. S. W. M. 6 yrs. Remained Yes No.

Referred by Dr Reynolds. Address Ypsilanti Mich. Admitted Dec 23 1901

Family History Mother had a cancer on breast, a brother cancer on hand. Both dying from this cause.

Personal History About 26 yrs ago had an attack had a lump both sides in the rt lumbar region. very painful to pressure, swelling in bowels and over the seat of pain. After about 4 wks after came to the rt of vomiting bowels and discharged into the rectum. very foul smelling. Pain left side, and discharged through the rectum 4-5 times. Pain at last ceased and the patient returned to work. Was sick with it nearly 2 yrs. She spoke of remaining sickness ceased 2 or 3 months following finish.

Menstrual: Age of appearance 13 Date of last period 1899. Regularity Usually Duration 3-4 days. Amount ... Color ... Clots Some. Pain Some dull Kind ... Where Some back.

Leucorrheal: Duration Some yrs. Amount ... Character ... Odor ...

Marital: Number of years married 5 Number of years widow 5. Number of children 0. Age oldest ... Age youngest ... Labor av. duration ... Instruments ... Abortions Date 1/2 1/3 0 ... month 1/2 1/3 0. Puerperal history 0.

Fig. 1.—The first page of the original hospital record of Mrs. H. H., a 64-year-old widow, who entered the University Hospital Dec. 23, 1901.

On March 12, 1902, Edmunds presented this material at the regular meeting of the Ann Arbor Medical Club, and in his discussion of the paper Cushny reiterated his belief in the identity of the clinically observed arrhythmia and experimental auricular fibrillation. He pointed out that in both conditions (compare Figs. 4 or 5 and 6) there was not only an irregularity with respect to sequence of pulses, but also in their amplitude. Thus, for example, in the upper tracing of Fig. 5, if one considers the downstrokes after any of the first few smooth upstrokes, one sees many small pulses which are irregular in sequence and amplitude. A comparison with the upper tracing of Fig. 6, which was taken from a dog during experimental auricular fibrillation, shows the same thing.

University of Michigan.

UNIVERSITY HOSPITAL. 581

DEPARTMEMT OF GYNECOLOGY.

NAME H. Mrs H. PAGE VI

CASE NO. 86 HOSPITAL NO. 998

Physical examination by Dr Peterson:

The abdomen is filled with a hard smooth solid tumor. The mass is partially divided into two lobes by a longitudinal sulcus which reaches from about 5" above pubes to 2" above umbilicus and 1½" to right of the latter. Just above pubes the lobes are fused together into one solid mass. The lobe on right is larger than that on right and reaches upwards to border of ribs, laterally it extends to within 1½" of anterior superior spines. The right lobe extends well over the right anterior superior spine but its upper border is about 1" from border of ribs. There is complete flatness over area occupied by tumor which is somewhat movable and non-sensitive.

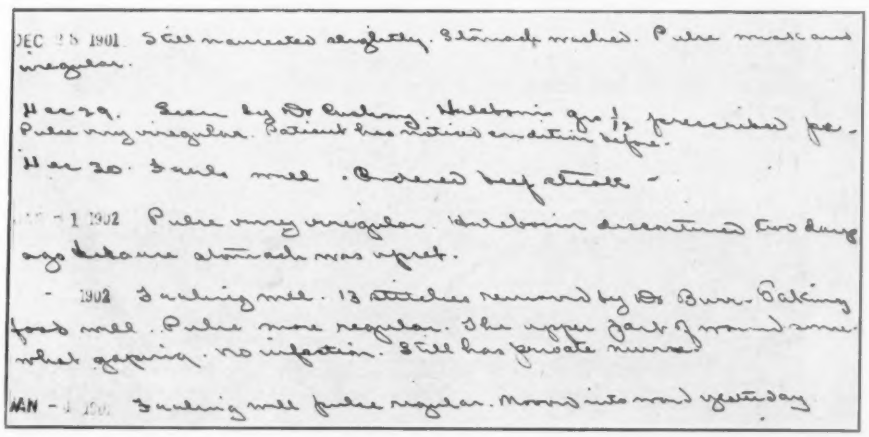
Vaginal examination

A small cervix can be made out pointing to left-anterior position and hard smooth masses about the size of Eng[lish] walnuts can be felt, each projecting from cervix at supravaginal junction. The uterus measures 2½" and seems to be directly continuous with tumor mass. When latter is moved the cervix moves also. The tumor can be felt projecting into pelvis on all sides of uterus.

Circumference of abdomen 1" below umbilicus = 37½"

Between anterior superior spines 1" below umbilicus = 16½"

Fig. 2.—The second page of the hospital record of Mrs. H., showing the physical examination as recorded by Dr. Edmunds.



DEC 28 1901 Still nauseated slightly. Stomach washed. Pulse weak and irregular.

Dec 29. Seen by Dr Cushny. Strychnine gr 1/2 prescribed pro. Pulse very irregular. Patient has retired and taken bitters.

Dec 30. Bowels well. Ordered beef steak.

[illegible] - 1 1902 Pulse very irregular. Strychnine discontinued two days ago. Abdomen stomach was upset.

- 1902 Bowels well. 13 stitches removed by Dr Burr. Eating food well. Pulse more regular. The upper part of wound somewhat gaping. No infection. Still has private nurse.

JAN - 1 190[illegible] Bowels well. Pulse regular. Moved into ward yesterday.

Fig. 3.—A portion of the daily progress notes kept on the patient. Note the examination by Dr. Cushny on December 29.

Unfortunately, the observations presented to the Ann Arbor Medical Club received practically no notice. The proceedings of this organization were irregularly recorded in the *Physician and Surgeon,* a medical journal published in Ann Arbor for several years, but the proceedings of this particular meeting were omitted. The result was that the paper which was presented in 1902 remained buried in obscurity. However, it has been possible to locate the original records of the Ann Arbor Medical

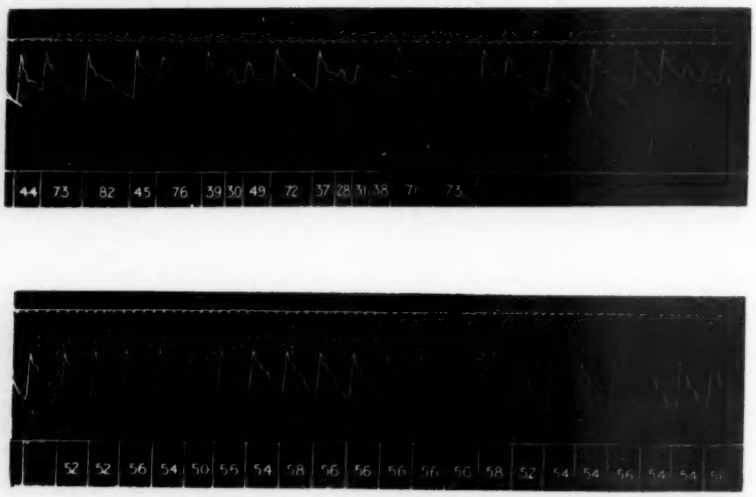


Fig. 4.—Pulse tracings made by means of the Jacquet sphygmograph on December 28. Upper tracing was made at 1:45 P.M., lower tracing at 2:45 P.M.

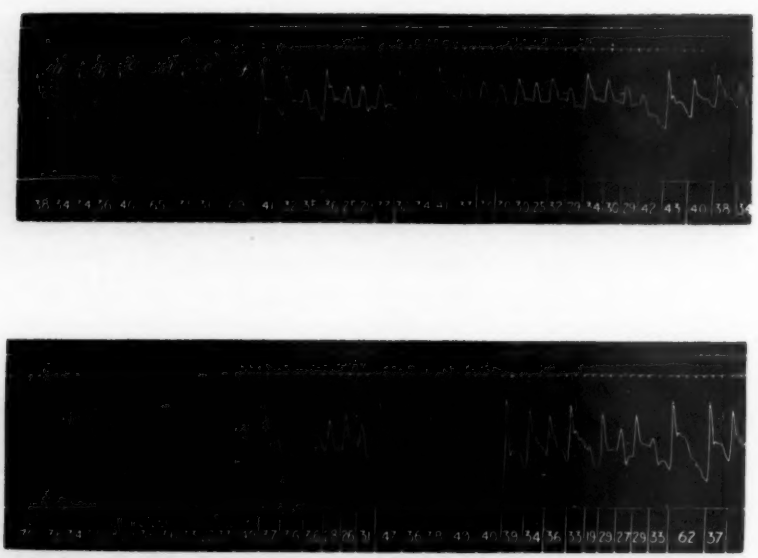


Fig. 5.—Further pulse tracings made on December 28. Upper tracing was made at 3:45 P.M., lower tracing at 4:45 P.M.

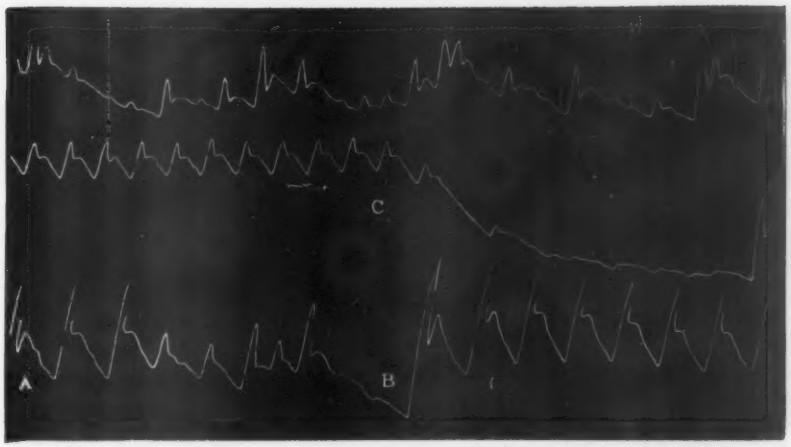


Fig. 6.—Tracings from carotid of dog made by means of Hürthle's tonometer. Uppermost tracing made during prolonged fibrillation. In middle tracing fibrillation was induced at *C*. In lowermost tracing there was imperfect fibrillation from *A* to *B*, no fibrillation after *B*.

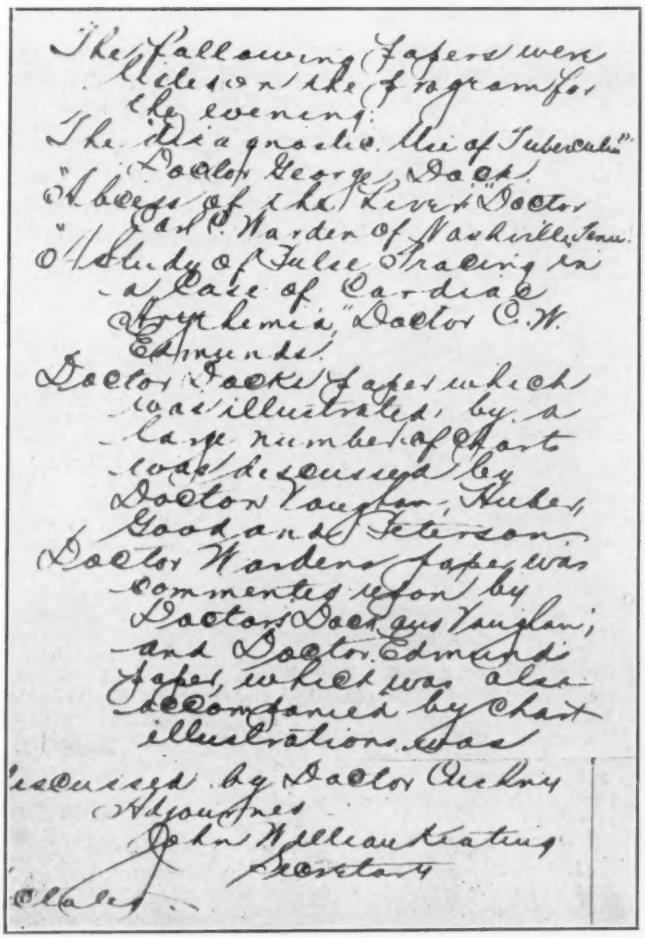

The following Papers were
Read on the Program for
the evening:
The "Diagnostic Use of Tuberculin"
Doctor George Dock.
"Abscess of the Liver" Doctor
Carl C. Warden of Nashville Tenn.
"A Study of Pulse Tracing in
a Case of Cardiac
Hypertrophy" Doctor C. W.
Edmunds.
Doctor Dock's Papers which
was illustrated by a
large number of Chart
was discussed by
Doctor Vaughan, Huber,
Goodall and Peterson.
Doctor Warden's Paper was
commented upon by
Doctors Dock, Vaughan,
and Doctor Edmunds.
Paper, which was also
accompanied by Chart
illustrations was
discussed by Doctor Cushny
Adjourned
John M. Gilleau Keating
Secretary

Fig. 7.—Page from record of Ann Arbor Medical Club, March 12, 1902, showing the papers given. Note the third paper read, and the notation at the end regarding the discussion by Dr. Cushny.

Club which were kept by the secretary. A portion is reproduced here (Fig. 7), and confirms the facts as given. Thus it will be seen (Fig. 7) that a meeting was held March 12, 1902, and that, in addition to several other papers, Dr. Charles Edmunds presented one, entitled "A Study of Pulse Tracings From a Case of Cardiac Arhythmia." In addition, the notation is made that Dr. Cushny discussed the paper and the accompanying pulse tracings that were presented. For a knowledge of what was said in the course of the discussion the author is indebted to the excellent memory of Dr. Edmunds. In addition, we have the later statement of Cushny[18] that he had reached the conclusions stated here as early as 1901.

We thus have evidence of the original and definite correlation of delirium cordis in man with experimental auricular fibrillation. It should be emphasized that this was accomplished seven years prior to the presentation of the final proof by Lewis and Rothberger and Winterberg that the two conditions are identical. The further history of this patient is of interest. As has been pointed out, the case, including the pulse tracings and conclusions, was finally reported in 1906, and again in 1907. The 1906 report[12] was rather obscure and passed unnoticed. Fox[19] further studied and reviewed this case. The patient was seen occasionally at the University Hospital for several years. When examined for the last time, in 1909, her cardiac irregularity had become permanent, and eventually she showed all the evidences of the cardiac failure which finally led to her death.

The author wishes to acknowledge gratefully the kind interest and valuable help of Dr. Arthur C. Curtis and Dr. Charles W. Edmunds in the preparation of this paper.

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THE ELECTROCARDIOGRAM IN THE AGED

A Study of 100 Men and Women Over the Age of 70 With Apparently Normal Hearts

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IN TREATING a large number of aged persons in whom no cardiac disease is apparent, one is struck by the unexpected frequency with which electrocardiographic abnormalities are found. Despite careful history and physical examination, which give no indications of heart disease, electrocardiographic study in many instances reveals marked changes. The present study was made to determine the number of supposedly normal people in the upper age groups whose electrocardiograms show definite changes—changes that are commonly accepted as indicative of a diseased heart. A follow-up study with autopsy material is not included in this paper. Willius[1] reviewed the electrocardiograms of 700 people over the age of 74 years. Fifty-five per cent had abnormal tracings. What proportion of his group had clinically normal hearts was not stated. Gelman and Brown[2] studied the electrocardiograms of 121 normal children between the ages of 12 and 14, as compared with a group of 60 "normals" over the age of 61. Of the latter group, the records showed a negative T_1 and T_2 in 10 per cent, and depression of S-T_1 and S-T_2 in 36 per cent (degree not stated). None of these changes occurred in the children. Their definition of "normal" was based on the absence of clinical manifestations of heart disease.

MATERIAL

The patients studied were chosen from the general medical clinic of the University of Minnesota. The group included only persons 71 years of age, or over, in whom no disease of the cardiovascular-renal system was evident, with the exception of the usual changes in the palpable vessels. Those selected fulfilled the following requirements: (1) A painstaking history elicited no symptoms of cardiovascular-renal disease; (2) the sensorium was clear, so that an accurate history could be obtained; (3) the blood pressure was not over 90 diastolic or 170 systolic; (4) physical examination showed no cardiac enlargement or diastolic murmur; (5) there was no evidence of syphilis, diabetes mellitus, or cerebral or acute infectious disease; (6) examination of the urine showed no evidence of renal disease; (7) chronic bronchitis, emphysema, and bronchial asthma were absent. All histories were taken, and physical examinations made, by the writer. Particular emphasis was placed on the history. The subjects selected were able to perform such tasks as walking two miles, washing clothes, running a household,

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or performing regular duties of a manual nature without dyspnea or a sense of tightness in the chest. None had attacks of nocturnal dyspnea.

They were further questioned concerning severe attacks of painless weakness, with sweating, which might suggest acute coronary occlusion. All these people stated that they were leading an active life, but at a slowed tempo. Prostatic symptoms, carcinoma of the skin, chronic arthritis, and diseases of the eye were the presenting complaints in over 90 per cent of the cases. Sixty-four were men, and 36 were women. Eighty-two were in the eighth decade, sixteen in the ninth, and two in the tenth.

The criteria of an abnormal electrocardiogram were: R-T or S-T segment elevated or depressed more than 1 mm. in relation to the isoelectric line; T waves diphasic, isoelectric, or inverted in Lead I or II, or both; QRS interval longer than 0.10 second; presence of a Pardee Q_3. Auricular fibrillation, P-wave changes, and alterations of the P-R interval were not included.

RESULTS

Twenty-six of these patients, sixteen men and ten women, showed an abnormal electrocardiogram, according to the above criteria. These abnormalities are summarized in Table I. The incidence in the various age groups will be seen in Table II. The sex incidence is essentially the same as that in the entire group. In the remaining seventy-four cases, premature beats were present in twenty-three, left axis deviation in fifty-nine, and right axis deviation in two.

COMMENT

It is well known that changes in the ventricular complex are not always identified with a diseased myocardium; also, myocardial disease is sometimes found when the tracing is normal. However, the electrocardiogram is invariably altered in the presence of severe heart muscle damage.[3] Consequently, the pronounced changes found in 26 per cent of our patients should be interpreted with the fact in mind that in rare instances the electrocardiogram is at variance with demonstrable heart lesions.

The frequency with which myocardial changes remain symptomless is well appreciated. In a series of articles devoted to the pathology of old age, Aschoff[4] cites the frequency of sudden death from coronary disease in old people who had boasted, "My heart is the healthiest organ in my body." Aschoff further states that the usual changes in senility, namely, brown pigmentation, increase in connective tissue, and fat deposits in the conduction system, are without effect on the electrocardiogram. Nathanson[5] reported a series of cases of coronary sclerosis in 37 per cent of which there was normal blood pressure, the heart was normal in size, and there was no cardiac insufficiency. Nathanson did not indicate how many of this group gave a history suggestive of coronary disease.

The frequency of asymptomatic coronary disease in the aged was pointed out by Gorham and Martin,[6] whose study revealed an increase

TABLE I

DETAILS OF THE 26 CASES IN WHICH THE ELECTROCARDIOGRAMS WERE ABNORMAL

CASE NO.	AGE	SEX	ADMISSION DIAGNOSIS	ELECTROCARDIOGRAPHIC CHANGES
8	77	F	Cataract	T_1 isoelectric. Low voltage—L. axis deviation.
9	73	M	Carcinoma of the face	T_1 and T_2 inverted. L. axis deviation.
2	72	M	Bladder stone	T_1 isoelectric. L. axis deviation.
4	80	M	Tumor of eyelid	QRS 0.14. QRS notched and slurred. L. axis deviation.
18	71	M	Tumor of face	QRS 0.14. QRS notched and slurred. Low voltage.
19	81	F	Cataract	QRS 0.12. L. axis deviation. Pardee Q_3.
24	74	M	Inguinal hernia	T_1 negative. Auricular fibrillation. L. axis deviation.
26	72	F	Chronic hyp. arthritis	S-T_1 and S-T_2 depressed. T_1 isoelectric.
32	75	F	Chronic hyp. arthritis	S-T_1 depressed. L. axis deviation. T_1 isoelectric.
35	76	F	Cataract	T_1 isoelectric. QRS 0.12.
36	76	M	Benign hypertrophy prostate	QRS 0.14. L. axis deviation.
37	77	M	Ca. stomach	T_1 isoelectric. L. axis deviation. Auricular fibrillation.
44	78	M	Benign hypertrophy prostate	QRS 0.12. Low voltage.
51	75	F	Carcinoma of the face	QRS 0.14. Rt. axis deviation.
53	71	F	Glaucoma	S-T_1 and S-T_2 depressed. T_1 and T_2 diphasic. L. axis deviation.
59	79	M	Chronic dermatitis	Right bundle branch block.
64	73	M	Benign hypertrophy prostate	S-T_1 depressed. T_1 inverted. L. axis deviation.
66	87	F	Cataract	QRS 0.12. S-T_1 elevated. L. axis deviation.
72	91	F	Cataract	T_2 and T_3 inverted. Rt. axis deviation.
73	71	M	Carcinoma of the face	S-T_1 and S-T_2 depressed. L. axis deviation.
78	71	F	Cataract	S-T_1 and S-T_2 depressed. L. axis deviation.
84	81	M	Benign hypertrophy prostate	Lt. bundle branch block.
86	76	M	Benign hypertrophy prostate	T_1 inverted. L. axis deviation.
87	85	M	Cataract	QRS 0.14. QRS notched and slurred.
91	71	M	Carcinoma of lip	Isoelectric T_1. Inverted T_2. Auricular fibrillation.
93	76	M	Benign hypertrophy prostate	T_1 isoelectric. S-T_1 depressed. Rt. axis deviation.

TABLE II

AGE DISTRIBUTION, BY DECADES, OF SUBJECTS WITH ABNORMAL ELECTROCARDIOGRAMS

AGES	CASES	ELECTROCARDIOGRAPHIC CHANGES	PER CENT
71-80	82	21	27.6
81-90	16	4	25.0
Over 90 (91 and 93)	2	1	50.0

in the number of painless coronary syndromes with advancing years. They found that painless occlusion and infarction are likely to result from slowly progressive fibrotic narrowing of the coronary vessels.

It is interesting to contrast the electrocardiographic findings in this old-age group with those in another group in which the ages ranged from 20 to 35. Shipley and Halloran[7] studied 200 normal men and women in the latter age group, using the same careful basis for selection as in the present series. Their subjects had normal blood pressure readings, normal physical findings, no history of cardiorenal disease, and good tolerance to exercise. The marked electrocardiographic changes occurring in 26 per cent of our aged subjects were not found in a single instance in this group of 200 younger people.

There is sufficient evidence that changes in the electrocardiogram take place normally in the ageing heart. These changes include a tendency for the action current to become more horizontal, for the voltage to decline, and for the T waves to be lowered, and toward an increase in the duration of the QRS and P-R intervals.[8] These moderate changes in the electrocardiographic pattern may or may not indicate lesions in the heart. The profound alterations which were found in 26 per cent of our cases cannot be regarded simply as a part of the process of senescence. It is believed proper to assume that they represent some abnormality of the heart. If a routine electrocardiographic study were made on aged patients who have no symptoms or signs of cardiac disturbances, it would be possible to recognize the fact that approximately one-fourth of them have heart disease.

SUMMARY

An electrocardiographic study was made on 100 men and women who, in so far as could be ascertained by a careful history and physical examination, had no heart disease. Eighty-two were in the eighth decade, sixteen in the ninth, and two in the tenth. Sixty-four were men, and thirty-six were women. Twenty-six per cent showed distinct electrocardiographic abnormalities. It is evident from this study that approximately 25 per cent of apparently healthy men and women over the age of 70 probably have considerable myocardial damage.

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NICOTINIC ACID: ITS ACTION ON THE PERIPHERAL VASCULAR SYSTEM

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NICOTINIC acid and its compounds have been used successfully in the treatment of canine black tongue,[1] pellagra,[2-5] and high-tone deafness.[6] Observers have been unanimous concerning the occurrence of a sensation of heat and flushing following the use of this drug. In each case, the reaction was of short duration, occurred within a few minutes after the ingestion of as little as 30 mg., and disappeared within thirty minutes. Spies, Bean, and Stone[3] found, in the majority of their cases, that this reaction coincides with an actual increase in the surface temperature of the face and neck, and a decrease in the temperature of the hands and feet.

In view of this apparent action on the peripheral blood vessels, the possibility that the drug might be used in the treatment of peripheral vascular diseases was investigated.

Fifteen adults were given 30 to 120 mg. of nicotinic acid by mouth. The effect on surface temperatures, oscillometer readings, pulse and respiratory rates, oral temperatures, and blood pressure was observed before, and from ten to thirty minutes after, the ingestion of the drug. The observations were made under standard conditions, after the subjects had rested for forty-five to sixty minutes in the recumbent position in a room kept at a constant temperature (70° F.). The body weights were all within normal limits. None of the subjects was acutely ill. There were nine women and six men in the series. Of these, four were normal; three had thromboangiitis obliterans; three, arteriosclerosis obliterans; one, essential hypertension; one, menopausal syndrome; and three, vasospastic disorders.

There were no prolonged untoward effects in any of the cases. Flushing and a sensation of heat, when they occurred, appeared in from seven to ten minutes, and disappeared within thirty minutes; they were more severe and lasting with the larger doses of the drug. Transitory tingling of the face and ears, itching, a sensation of heat over the arms and back, and slight dizziness were noted occasionally. There was no appreciable effect on blood pressure except in two cases, in which it was markedly lowered. In no instance was it raised. Respiratory and pulse rates and oral temperatures varied slightly. From the tabulation it can be seen that, regardless of the amount of the drug and the condition of the patient, surface temperatures were very inconstant. Reddening and flushing of the skin may occur with

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TABLE I

EXPERIMENTAL OBSERVATIONS

RESPIRATORY AND PULSE RATES, ORAL TEMPERATURE, AND BLOOD PRESSURE DID NOT CHANGE, OR CHANGED ONLY SLIGHTLY, UNCHANGED OR MINIMAL UNLESS OTHERWISE STATED

CASE	AGE AND SEX	DOSE	DIAGNOSIS	SURFACE TEMPERATURES	OSCILLOMETER READINGS	REACTIONS
1	50 F	30 mg.	Normal	Face, fingers, toes unchanged.	Slight decrease in both calves and ankles, 0.1 to 0.8 division points.	None.
2	35 F	30 mg.	Normal	Face increased 1.4 to 1.8° Cent. Fingers showed slight increases and decreases. Toes decreased 0.1 to 2.0° C.	Calves unchanged. Ankles decreased 0.4 to 0.5 div. points.	Face flushed with sensation of heat.
3	40 F	60 mg.	Vasospastic disorder of hands (Raynaud's Syndrome).	Face decreased 0.2 to 0.5° C. Fingers decreased 0.5 to 2.0° C. Toes decreased 0.1 to 1.0° Cent.	Left calf, ankle no change. Right calf and ankle decreased 0.5 to 1.4 division points.	None.
4	50 M	60 mg.	Thromboangiitis obliterans.	Face and fingers no change. Toes decreased 0.3 to 1.6° C.	No change except left ankle decreased 1.3 division points.	Flushing of face with tingling. Oral temp. reduced from 98.2°F. to 97.4°F.
5	20 F	80 mg.	Normal.	Face increased 0.5 to 0.7° C. Fingers decreased 0 to 1.2° C. Toes decreased 0 to 0.6° C.	All decreased from 0.1 to 1.5 division points (Fig. 1).	Entire right half of body to the knee, flushed, warm with itching. Left side, neck was warm.
6	60 M	80 mg.	Hypertension. Arteriosclerosis obliterans.	Not done.	Right arm decreased 3.3 div. pts. Both calves unchanged. (Fig. 1.)	Slight itching and flushing of face. Blood pressure dropped from 225/113 to 160/95.
7	16 F	80 mg.	Vasospastic disorder of feet.	Face decreased 0.9 to 1.8° C. Fingers increased 0 to 2.0° C. Toes decreased 0 to 1.5° C.	All decreased 0.2 to 1.9 div. points. (Fig. 2.)	None except for flushing of forehead with sensation of cold.
8	35 F	100 mg.	Vasospastic disorder of hands (Raynaud's syndrome).	Face increased 0.5 to 1.5° C. Fingers decreased 0.8 to 3.0° C. Toes decreased 0.2 to 1.1° Cent.	No change except for very slight decreases.	Flushing of face with itching and tingling.

TABLE I—CONT'D

CASE	AGE AND SEX	DOSE	DIAGNOSIS	SURFACE TEMPERATURES	OSCILLOMETER READINGS	REACTIONS
9	63 M	100 mg.	Arteriosclerosis obliterans.	Face increased 0 to 0.7° C. Fingers decreased 0.8 to 3.0° C. Toes increased 0.1 to 1.3° Cent.	Not done.	Flushing of face with itching and tingling.
10	61 M	100 mg.	Arteriosclerosis obliterans.	Face decreased 0.4 to 1.2° C. Fingers increased 1.3 to 1.8° C. Toes unchanged.	Left ankle and right calf unchanged. Right ankle and left calf decreased 1.0 div. points.	Flushing of face with itching and tingling.
11	45 M	100 mg.	Thromboangiitis obliterans.	Face decreased 0.4 to 0.6° C. Fingers and toes very slight changes.	Right calf increased 0.2 div. pt. Left calf increased 0.5 div. pt. (Fig. 2.)	None.
12	50 F	100 mg.	Essential hypertension.	Not done.	Not done.	Blood press. dropped from 190/100 to 110/80 within 20 minutes. Pulse remaining 64, weak and thready. Near collapse.
13	45 F	100 mg.	Menopausal syndrome.	Not done.	Left arm unchanged. Left calf increased 1.0 div. pt. Right calf decreased 1.5 div. point.	None
14	32 F	120 mg.	Normal.	Face decreased 0.6 to 1.5° C. Fingers-thumbs decreased 0.2 to 3.4° C. and little fingers increased 0.3 to 1.6° C. Toes decreased 0.5 to 1.7° Cent.	All decreased 1.2 to 2.5 div. points (Fig. 3).	Nausea within 6 minutes. Face, arms, legs became flushed resembling a sunburn with marked itching. Chills. Oral temp. dropped from 98.6° F. to 98° F. Malaise present.
15	49 M	120 mg.	Thromboangiitis obliterans. (Lumbar sympathectomy 8 years previously.)	Face increased 0.5 to 0.6° C. Fingers increased 1.1 to 2.6° C. Toes increased 0.1 to 1.6° Cent.	All decreased 0.2 to 2.0 div. points (Fig. 4).	Face flushed.

either an increase or decrease in surface temperature, with or without the sensation of warmth. In Cases 7 and 14 the face became red and flushed, but the surface temperature decreased, and the sensation was one of cold. The amplitude of the oscillometric tracings diminished in the majority of the cases, particularly when large doses of the

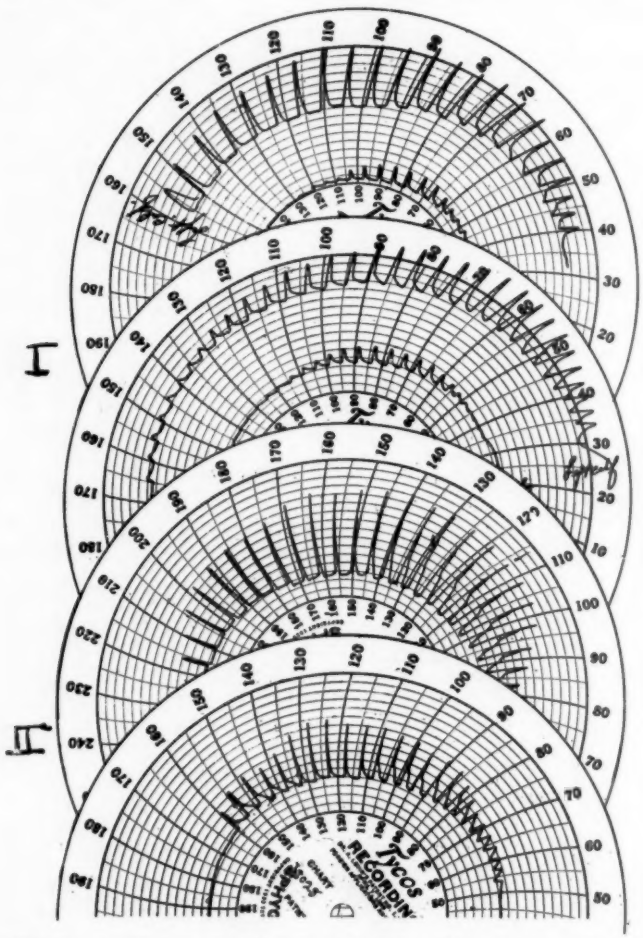

Fig. 1.—Graphs I. Upper chart: left calf and ankle at rest. Lower chart: 15 minutes after 80 Mg. nicotinic acid. Marked reduction of amplitude of tracing from first reading in calf. Subject was a normal woman, 20 years old.
Graphs II. Upper chart: right arm at rest. Lower chart: 10 minutes after 80 Mg. nicotinic acid. Blood pressure dropped from 225/113 to 160/95, as shown in the tracing. Subject was a 60-year-old man, suffering from hypertension and arteriosclerosis obliterans.

drug were used. The diminution varied from slight to marked in eleven of the thirteen cases in which tracings were recorded. These changes were not absolutely consistent. In two cases there was a definite increase in amplitude. Untoward reactions, while alarming in one subject (Case 12), were of short duration. One subject (Case 14) was rendered extremely uncomfortable by chills and a fall of body

temperature. In all of the subjects the effects of the drug had disappeared completely within thirty to forty minutes. In many instances the peak of the reaction was very short, lasting less than ten minutes.

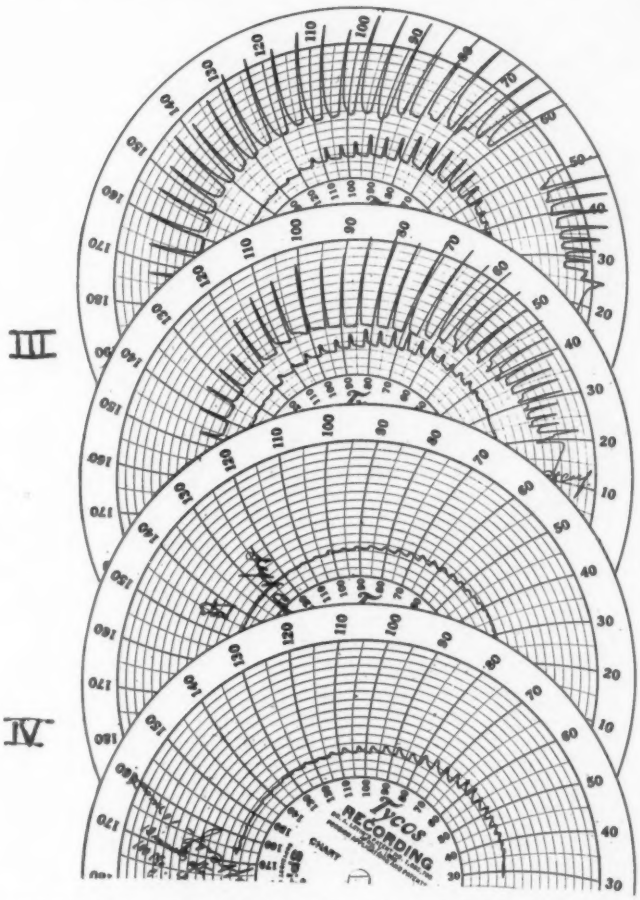

Fig. 2.—Graphs III. Upper chart: right calf and ankle at rest. Lower chart: 15 minutes after 80 Mg. nicotinic acid. Generalized reduction in amplitude. Patient was a girl, 16 years old, suffering from severe Raynaud's disease of the lower extremities.

Graphs IV. Upper chart: left calf at rest. Lower chart: 15 minutes after 100 Mg. nicotinic acid. This was one case in which increased pulsation occurred. Patient was a man, 45 years old, suffering from thromboangiitis obliterans.

COMMENT

The discordant results are difficult to explain. Other observers[3, 4] have noted surface-temperature changes, cardiovascular and gastrointestinal symptoms, substernal oppression, and pruritus or other skin manifestations. They have attributed some of their findings to a histamine or a parasympathetic action of the nicotinic acid. The discordant results of this study may have been due to individual differences in susceptibility, to variations in the rate of absorption of the

drug from the gastrointestinal tract, and to the fact that the observations, especially the surface temperature measurements, were made at certain arbitrarily selected times.

Although it is difficult to reconcile the decreased oscillometric readings and the occasional marked fall in blood pressure with a parasympathetic effect, a histamine[7] action does apparently account for most of the phenomena observed. Many unrelated substances

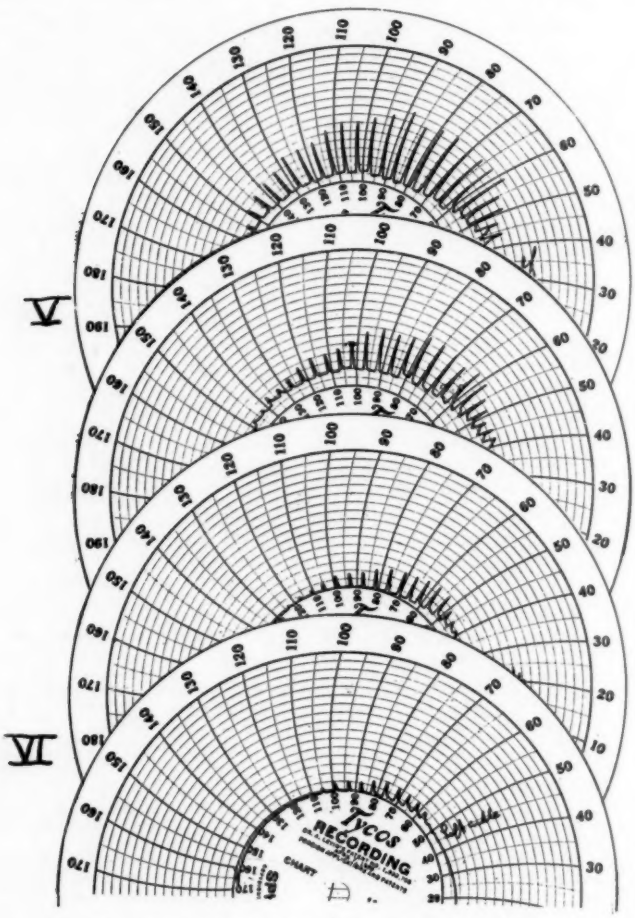

Fig. 3.—Graphs V. Upper chart: right calf at rest. Lower chart: 15 minutes after 120 Mg. nicotinic acid.
Graphs VI. Upper chart: left ankle at rest. Lower: 15 minutes after 120 Mg. nicotinic acid.
All pulsations were reduced in amplitude. These recordings were from the same subject, a normal woman, 32 years of age.

give this reaction. They include tissue extracts, secretin, peptones and other products of protein cleavage, blood serum, and bacterial products. It also occurs in traumatic shock. Histamine causes a contraction of smooth muscle regardless of its innervation, and an increased permeability and dilatation of the capillary bed. This action

is clearly apparent in the majority of the cases observed, and occurs even after sympathectomy (Case 15). Substernal oppression may be the result of coronary artery constriction, although electrocardiographic tracings have been reported to show nothing abnormal.[3] The lowered surface temperature observed when the skin is flushed and red may be due to stasis of blood in the engorged capillary bed. A further pharmacologic action of histamine is an initial stimulation

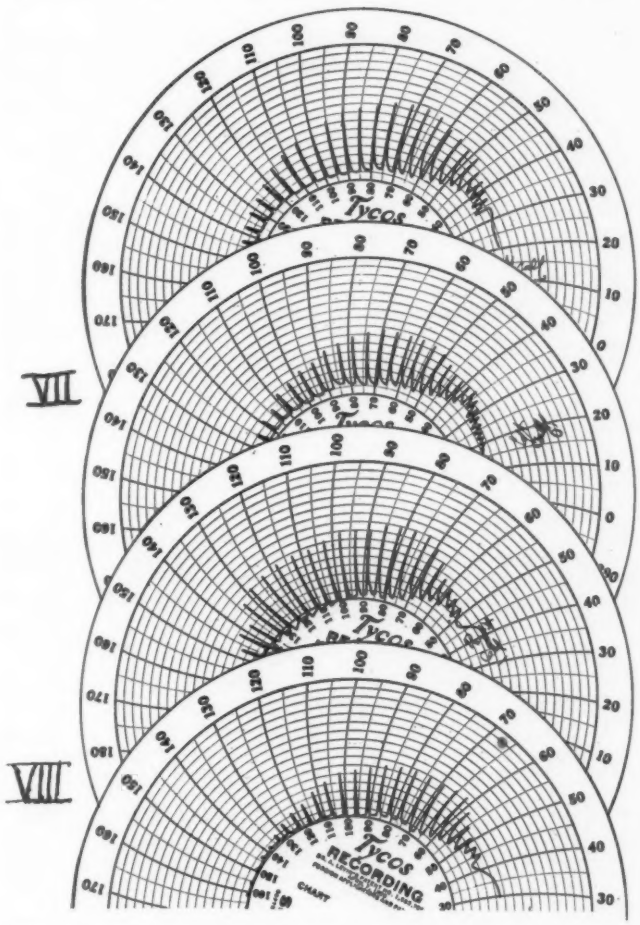

Fig. 4.—Graphs VII. Upper chart: left calf at rest. Lower: 15 minutes after 120 Mg. nicotinic acid.

Graphs VIII. Tracings from right calf, before and after nicotinic acid, in the same individual. All pulsations are reduced in amplitude. Patient was a man, 49 years old, suffering from thromboangiitis obliterans. He had had a lumbar sympathectomy eight years previously.

of the gastrointestinal tract, followed by a relaxation. This may explain the nausea, vomiting, belching, and other gastrointestinal symptoms reported by most observers. Spies, et al.,[3] injected nicotinic acid intracutaneously in normal subjects, thereby obtaining wheals and pruritus which were similar to those produced by histamine.

SUMMARY

1. Nicotinic acid, administered orally, in single doses, in the majority of cases causes transitory flushing of the skin, tingling, itching, and sensations of heat, regardless of the condition of the subject or the size of the dose.

2. The changes in the surface temperature of the face, fingers, and toes are variable and unpredictable.

3. The amplitude of the oscillometric tracings is diminished in the majority of cases, and the degree of diminution varies directly with the quantity administered.

4. It is suggested that the effects of nicotinic acid are similar to those produced by histamine.

5. Nicotinic acid is of little value in the treatment of peripheral vascular disease because it produces uncomfortable symptoms and arterial constriction, and because whatever favorable effects it may have are of very short duration.

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THE INCIDENCE OF ORGANIC HEART DISEASE IN SCHOOL CHILDREN*

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MANY surveys to determine the incidence of heart disease in school children have been conducted in various parts of the United States. We have examined the children of the Cincinnati schools in order to compare the incidence of organic heart disease in this city with that of other communities. In localities where rheumatic fever is prevalent, about 80 per cent of the children with organic heart disease have rheumatic valvulitis, and the remainder, congenital lesions. This ratio has been accepted so frequently that we believed it wise to investigate the point further in a community such as ours, where rheumatic fever is less severe than in many eastern and northern cities.

Since a previous survey of the same type, but on a smaller scale, had been conducted in this city in 1927, by Benjamin,[1] we were anxious to observe any changes of incidence rates which might have occurred during the interval of 10 years.

PROCEDURE

During a 2-year period, beginning in the fall of 1936, the school physicians referred for special examinations all children whom they suspected of having any cardiac abnormality. This group of patients was re-examined by one of four pediatricians, all of whom were especially interested in cardiology and were attending physicians to the Children's or General Hospital cardiac clinic. The children were stripped to the waist and examined in the reclining and sitting positions, and in the standing position before and after exercise. The examination included percussion and auscultation of the heart, determination of the heart rate and blood pressure, estimation of the nutritional status, inspection of the mouth and throat, palpation for tonsillar lymph nodes, and observation for cyanosis and clubbing of fingers. Electrocardiograms, teleoroentgenograms, and fluoroscopic examinations were obtained in doubtful cases whenever possible. Historical data, obtained from the parents by visits of the school nurse to their homes, included the age at which heart disease was first noted, the occurrence of cyanosis or cyanotic attacks, symptoms of the rheumatic state, and whether the child had had a tonsillectomy, diphtheria, or scarlet fever.

RESULTS

Incidence.—A total of 85,389 children in 157 schools were examined by the school physicians during the 2-year period, and 1,782 of these children had some clinical finding suggestive of heart disease. When

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this group was re-examined by us, 633 were found to have normal hearts, 700 to have murmurs which were believed to be only functional or accidental in type, and 449 to have definite evidence of cardiac disease. This last group constituted 25.4 per cent of the patients selected by the school physicians, or 0.53 per cent of the entire number of children (Table I).

TABLE I

THE INCIDENCE OF CARDIAC LESIONS IN SCHOOL CHILDREN

I. Total number examined by school physicians				85,389	
Public elementary schools			43,146		
Catholic elementary schools			17,565		
Public junior and senior high schools			19,047		
Catholic high schools			2,008		
Special and trade schools			3,623		
II. Number with suspected heart disease				1,782	2.09%
III. Reclassification, at special examination, of these 1,782 patients.					
Normal hearts			633—35.5%		
Functional or accidental murmur			700—39.2%		
Abnormal hearts			449—25.2%		
IV. Number with definite evidence of heart disease				449	0.53%
A. Organic			304		0.36%
Acquired	170	55%			0.20%
Congenital	131	45%			0.15%
Unclassified	3	--		less than	0.01%
B. Possibly organic (Class E)			109		0.12%
Possibly acquired		81			0.09%
Possibly congenital		28			0.03%
C. Extrasystoles (5 included in above categories also)			41		0.04%

Children with tachycardia and hypertension were not included in the group with cardiac lesions because of the great lability of the pulse rates and blood pressures of children under conditions of excitement and fear. From single examinations, the diagnosis of these abnormalities did not seem justifiable.

Of the 449 children with heart disease, 304 had definite evidence of organic lesions (0.36 per cent of the total number of 85,389 children); 109 were classified as possibly having organic disease but requiring further observation to complete the diagnosis; and 41 had extrasystoles (Table I). The diagnosis of "potential heart disease" was purposely omitted because of the lack of complete histories in each case.

Race, Sex, and Age Distribution.—The incidence of *acquired heart disease* was found to be almost twice as high among the colored children as among the white children (Table II). This difference was shown to be statistically significant (employing a fourfold table and the Chi square formula). This is contrary to the observations of other investigators. Wood, Jones, and Kimbrough[2] found rheumatic heart disease less common among the negro population of Virginia than among the white population. Wilson, Lingg, and Croxford[3] analyzed the records of 500 chil-

dren attending the heart clinic at Nursery and Child's Hospital in New York City. Although this clinic drew its patients from a negro district, only 4.6 per cent of the children enrolled as cardiac patients were negroes. Sutton[4] found that the percentage of negro children in the general pediatric clinic of Bellevue Hospital, New York City, was three times that in the clinic for patients with heart disease. Ash,[5] in a study of the records of all rheumatic patients treated in the wards or heart clinic, over a ten-year period, at the Children's Hospital in Philadelphia, found that 83 per cent of the rheumatic patients were white, and 17 per cent were negroes, while among the total number of all patients in the dispensary and wards of the hospital the distribution between the two races was equal.

Acquired heart disease was more common in girls than in boys (Table II).

TABLE II

RACE, SEX, AND AGE DISTRIBUTION

	TOTAL NUMBER SCHOOL CHILDREN	ACQUIRED LESIONS NUMBER	ACQUIRED LESIONS PER CENT	CONGENITAL LESIONS NUMBER	CONGENITAL LESIONS PER CENT
Race					
White	73,074	191	0.26	140	0.19
Black	12,315	60	0.49	19	0.15
Total	85,389	251	0.29	159	0.19
Sex					
Male		114	(45.4 per cent of 251)	80	(50 per cent of 159)
Female		137	(54.6 per cent of 251)	79	(50 per cent of 159)
Total		251		159	
Age					
5- 9 yr.	23,995	13	0.054	38	0.158
10-14 yr.	26,536	75	0.282	46	0.172
15-18 yr.	14,369	48	0.333	22	0.153
Total	64,900	136		106	

Data in regard to age distribution could be obtained only from the public schools. The low incidence of acquired heart disease in the group under 10 years of age and the highest incidence in children of high school age were to be expected.

Congenital heart disease was fairly equally divided among the race, sex, and age groups (Table II).

Histories.—An analysis of the histories of the children with acquired heart disease indicated that 66 per cent of children with definite cardiac lesions had had one or more rheumatic symptoms, while only 3.6 per cent of the children with doubtful lesions had had similar symptoms (Table III). Negative histories were much more frequent (36.1 per cent) in the doubtful cases than in those in which there were definite cardiac lesions (8.9 per cent).

TABLE III

HISTORIES OF CHILDREN WITH ACQUIRED HEART DISEASE

	ACQUIRED HEART DISEASE		POSSIBLY ACQUIRED HEART DISEASE	
	NO. PTS.	PER CENT	NO. PTS.	PER CENT
Rheumatic fever (chiefly polyarthritis)	89	52.3	1	1.2
Chorea	9	5.2	2	2.4
			66.0	
Rheumatic fever and chorea	10	5.8	-	-
Chorea and growing pains	4	2.3	-	-
Growing pains only	17	10.0	14	17.2
Tonsillitis only	9	5.2	12	14.8
Scarlet fever	6	3.3	7	8.6
Heart disease noted following infections, such as grippe and pneumonia			2	2.4
History negative	15	8.9	29	36.1
No history available	11	6.4	14	17.2
Total	170		81	

Interesting to note in the histories of the children with congenital heart lesions is the fact that in about 55 per cent the condition was noted at birth or during the first two years of life, and that in 24 per cent the condition was not detected until school age (Table IV).

TABLE IV

HISTORIES OF CHILDREN WITH CONGENITAL HEART LESIONS

TIME HEART DISEASE WAS NOTED	NUMBER OF CHILDREN	PER CENT
At birth	28	29.4
Between first month and second year	24	25.2
During third year	5	5.3
During fourth year	5	5.3
During fifth year	10	10.5
After fifth year	23	24.2
Total	95	
No history available	36	
Total	131	

Economic Levels.—It was possible to group the children with acquired heart disease into four economic levels, according to small census tracts which have been outlined in this city. Group one had the lowest economic status, and group four the highest. A total of 146 cardiac children, 10 to 19 years of age, was compared with the total population of the same age in the respective economic locations, employing the figures of the 1935 census. The mean incidence rate of acquired heart disease for the entire group was 0.20 per cent, and the probable error was $\pm$ .029. When we consider the individual groups, it is obvious that the incidence rates at the two lowest economic levels were significantly high, that the rate for the group with the highest economic status was significantly low, and that that of the third group falls so close to the standard deviation that it is probably not significant (Table VIII).

Anatomic Diagnoses.—Of the 170 children with acquired heart disease, 68 per cent had mitral insufficiency alone. A diagnosis of mitral insuf-

ficiency was made on the basis of a systolic murmur at the apex transmitted toward or into the axilla, and persisting or increasing in intensity on change of position from the reclining to the erect position and after exercise. In none of these patients was a diastolic murmur present. A list of all of the diagnoses is given in Table V.

Of the 131 children with congenital heart disease, even with the aid of fluoroscopy and electrocardiography, an anatomic diagnosis was impossible in thirty-two. Patent ductus arteriosus was diagnosed in 25.1 per cent of the cases, and interventricular septal defects in 38.1 per cent. The latter group represents those cases in which a fairly rough, long, loud, high-pitched systolic murmur was heard over the precordium, loudest in the third or fourth intercostal space just to the left of, or over, the sternum, with or without the accompaniment of a thrill. It is quite possible that in some instances this anatomic diagnosis was incorrect. Of the children with congenital lesions, cyanosis was slight in eight instances, moderate in five, and marked in six.

Medical Care.—The type of medical care of 413 children (excluding those with premature contractions) is shown in Table VII. There were 39.0 per cent who were under the care of private physicians, 9.2 per cent who had received no medical attention at the time of the survey, and the remainder were being observed and treated in heart clinics or special schools and institutions.

TABLE V

ANATOMIC DIAGNOSES IN CHILDREN WITH ACQUIRED HEART DISEASE

	NUMBER	
Mitral insufficiency	116	68%
Mitral stenosis	2	
Mitral insufficiency and stenosis	15	
Mitral insufficiency and probably stenosis	7	
Mitral insufficiency and aortic insufficiency	9	
Mitral insufficiency and aortic stenosis	1	
Mitral insufficiency and stenosis and aortic insufficiency	5	
Aortic insufficiency	8	
Aortic insufficiency and stenosis and possibly mitral insufficiency and stenosis	3	
Mitral insufficiency and stenosis and aortic stenosis	1	
Intraventricular block	1	
Mitral insufficiency and stenosis and tricuspid insufficiency	1	
Rheumatic heart disease—anatomic diagnosis not known (refused examination)	1	
Total	170	

Control Study.—At the completion of the survey it was felt that some further study of the validity of our statistics should be attempted. For this purpose an elementary school representing a fair cross section of economic levels was chosen, and the four special clinicians examined every child in the school, from the kindergarten class through the eighth grade.

Of a total of 709 children examined, four were found to have definite signs of organic heart disease, and five others had to be classified as hav-

TABLE VI

ANATOMIC DIAGNOSES IN CHILDREN WITH CONGENITAL HEART DISEASE

	NUMBER	PER CENT
Dextrocardia	2	1.5
Dextrocardia and pulmonary stenosis	1	0.8
Interventricular septal defect	50	38.1
Interventricular septal defect and possibly heart block	1	0.8
Patent ductus arteriosus	33	25.1
Patent ductus and rheumatic heart disease—mitral insufficiency	1	0.8
Septal defect and patent ductus	2	1.5
Aortic stenosis	1	0.8
Pulmonary stenosis	7	5.3
Pulmonary stenosis or patent ductus	1	0.8
No diagnosis	32	24.4
Total	131	

TABLE VII

MEDICAL CARE OF 413 CHILDREN

	PRIVATE PHYSICIAN	NO PHYSICIAN	CONDON* SCHOOL	FREE CLINICS
Acquired	42	12	28	88
Congenital	65	8	19	39
Possibly acquired	40	12		29
Possibly congenital	15	6		7
Unclassified			2	1
Total	162	38	49	164
Per cent	39.0	9.2	51.8	

*Special school for handicapped children.

TABLE VIII

MORBIDITY RATES IN ACQUIRED HEART DISEASE IN THE SCHOOL SURVEY, CLASSIFIED ACCORDING TO ECONOMIC STATUS OF THE POPULATION

ECONOMIC STATUS	CHILD POPULATION 10 TO 19 YEARS OF AGE	PATIENTS 10 TO 19 YEARS OF AGE	PER CENT
Group 1 (lowest level)	19,481	62	0.32
Group 2	13,501	48	0.26
Group 3	17,987	26	0.14
Group 4 (highest level)	15,843	10	0.063

ing "possible organic heart disease" (Class E). When the figures of incidence in this group were compared with those of the entire survey, the statistical analysis indicated that the incidence of organic heart disease in the control sample was not significantly greater than that in the entire survey, but a significantly greater number of children with "possible heart disease" were uncovered in the control sample than in the general survey. It is possible, therefore, that the incidence of borderline cases, classified as "possible heart disease," in our general survey is too low. The school physicians in their routine examinations of children may have overlooked some of the minor cardiac defects. This may perhaps be explained by the following facts: (a) the school examinations have, until recently, been made with the children's clothes loosened, but

TABLE IX

INCIDENCE OF HEART DISEASE IN SCHOOL CHILDREN OF OTHER CITIES
(REPORTS ARRANGED IN CHRONOLOGICAL ORDER)

		TOTAL SCHOOL POPULATION EXAMINED	ORGANIC HEART DISEASE PER CENT	RHEUMATIC HEART DISEASE PER CENT
New York City, 1915[6]		278,174	1.50	
New York City, 1918[7]		250,000	1.60	1.28 *
New York City, 1918 to 22[7]		1,336,343	1.39	1.112*
New York City, 1921[8]		44,000	0.50	0.40 *
Chicago, 1923[7]		158,826	0.90	0.720*
Philadelphia, 1924[9]		23,671	0.63	0.504*
Chicago, 1924[7]		153,671	1.50	1.20 *
Chicago, 1925[7]		130,260	1.70	1.36 *
Boston, 1927[10]		119,337	0.52	0.45
Philadelphia, 1929[11]		10,333 (B)	0.91	0.76
Florida, Illinois and Missouri, 1929[12]		17,974	1.00	0.80 *
Cincinnati, 1927[1]		6,960	0.37	0.296*
Rochester, Minn., 1931[13]		1,328 (A)	0.70	0.560
New York City, 1931[14]		2,691 (C)	1.10	0.88 *
New Haven, 1934[15]				
	Grade	*Children*	(Systolic Murmur)	
"Better School"	1	1,144	1.32	1.05 *
	5	1,123	1.42	1.13 *
"Poorer School"	1	1,863	1.93	1.54 *
	5	1,628	2.08	1.68 *
Philadelphia, 1937[16]				
(Elementary)		33,293	0.50	
			(E) 0.30	
			(F) 0.12	
(High School)		9,154	0.90	
			(E) 0.40	
			(F) 0.20	
New Mexican Indians, 1937[17]		1,019	--	0.50
Northern Indians, 1937[17]		688	--	4.50
San Francisco, 1938[18]		13,338	0.37	0.22
Cincinnati, 1938		85,389	0.36	0.20
			(E) 0.12	

*Rheumatic heart disease computed as 80 per cent of all organic cases.
(A) Ages 11 to 20
(B) Ages 6 to 18
(C) Ages 14 17
(E) "Possible heart disease"
(F) "Potential heart disease."

not removed, (b) the examinations have been made with the children in the standing position only, and (c) it is possible that insufficient attention has been paid to the heart in routine school examinations. It must be remembered, also, that the four clinicians participating in this survey were pediatricians with special training in cardiology, who were looking for abnormal cardiac signs, and were able to examine each child with extreme care.

COMMENT

In many of the school surveys of this type, no attempt has been made to divide the cases of organic heart disease into acquired and congenital groups; it was simply assumed that 80 per cent of all organic heart disease was rheumatic in origin, regardless of geographic location. These

figures were derived from the examination of children in the second decade of life who were living in the eastern part of the United States,[19] and have been applied unjustifiably to conditions in other localities. This proportion of 80 per cent rheumatic heart disease does not hold true among the school children of Cincinnati, where only 55 per cent of the cases of organic heart disease could be classified as acquired, or rheumatic, in origin. The statistics from San Francisco,[18] where 65.0 per cent of the organic heart disease of school children was found to be rheumatic in type, corresponded most closely to ours.

The variation in the statistics from other localities is evident (Table IX). The results depend upon the examiners, the age of the children examined, the economic status of the children, and the climate or locality in which the children live. For example, the Boston survey[10] was carried out in much the same way as ours, with cardiologists as the special examiners. The comparatively low incidence of organic heart disease found (0.52 per cent) is of interest. In the New Haven survey,[15] the higher incidence of acquired heart disease in the "poorer school" is well illustrated. In the Philadelphia survey[16] of 1937, the higher incidence of acquired heart disease among the high school students was considerable. The difference in incidence of acquired heart disease which depends on climate is illustrated in the survey carried on among the New Mexican and Northern Indians.[17] The incidence among the Northern Indians was nine times higher than that among the New Mexican Indians. Our figures agree closely with those of the survey previously carried out in this city,[1] except in respect to etiology. In the previous study, acquired heart disease had been assumed to constitute 80 per cent of all organic heart disease in children in the second decade of life.

SUMMARY

1. Of a total of 85,389 children, 5 to 19 years of age, who were examined by school physicians, 1,782 were suspected of having heart disease.

2. Re-examination of this group of 1,782 by a group of pediatricians indicated that 449 (0.53 per cent of the total school population) had organic lesions, and 700 others had functional or accidental murmurs. The remaining 633 children had normal hearts.

3. Of the 301 children with organic lesions, acquired heart disease, probably rheumatic in origin, occurred in 55 per cent, and congenital lesions in 45 per cent.

4. Acquired heart disease was more prevalent in the negro than in the white race. It occurred more frequently in girls than in boys, and more often in children living under poorer economic conditions than in those whose economic status was better. The incidence of congenital heart disease was independent of race or sex, and was fairly equally distributed among the different age groups studied.

5. About 24 per cent of the parents of children with congenital heart disease had been totally unaware of the existence of these lesions until the school examinations were made.

6. The results of cardiac examinations by the school physicians were compared with those made by a special group of pediatricians in a sample of the school population. Both groups discovered approximately the same number of children with definite lesions, but the physicians especially interested in cardiology detected more borderline cases of "possible heart disease."

7. A comparison of the results of this study with previous school surveys indicates that there are wide variations of incidence in different localities. The statement that 80 per cent of the acquired lesions are rheumatic in origin is true only in areas where rheumatic fever is prevalent and severe, and cannot be universally employed as a distribution figure.

I wish to express my gratitude to my colleagues who aided in the examinations, Doctors Margaret Posey, Carl Koch, and Irvin Itkoff. In addition, I wish to thank Mrs. Catherine Kavel, nurse to the cardiac clinics, who visited the schools with us, for her untiring efforts; Miss Minnie Landon, for aid in the compilation of statistics; Mrs. William Brown, for her assistance in the statistical analysis; Dr. Floyd Allen, for preparing the data on the economic distribution of the patients; Dr. Julien Benjamin, for his help and advice; Doctor Harder, Acting Health Commissioner, and the School Physicians, for their cooperation; and Mrs. Tooker and the Board of Health nurses, for their help in the school examinations and for obtaining histories in the cardiac cases.

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A COMPARATIVE STUDY OF PRECORDIAL LEADS IV R AND IV F

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THE rapidly spreading use in recent years of supplementary precordial leads in clinical electrocardiography was unfortunately attended by much confusion arising from lack of uniformity in technique and nomenclature. In an effort to standardize practice, committees of the American Heart Association and the Cardiac Society of Great Britain and Ireland, early in 1938, jointly recommended the general adoption of a uniform apical placement of the precordial electrode, and further suggested that for all ordinary purposes the precordial (exploring) electrode be paired either with one on the right arm (lead to be known as IV R) or the left leg (lead to be known as IV F). The galvanometer connections of the latter lead were to be so made that relative positivity of the apical electrode would be represented in the finished curve by an upward deflection.[1]

At the time these recommendations were made, the relative merits of Leads IV R and IV F were not yet considered established, and the committee implied that further investigation was required before one or the other could be recommended for routine clinical use.

It had been the practice for several years in this laboratory to employ a lead practically identical with Lead IV R. However, casual experiments with other leads, including IV F, indicated that occasionally significant discrepancies were encountered even between these two leads. Although convenience favored Lead IV R, since it involved only the arm leads and required no interchanging of the electrodes, it was evident that the relative clinical value of each of these leads required further clarification, and this need was considered the more urgent when the universal adoption of *either* Lead IV R *or* Lead IV F was recommended. This study was thus undertaken with the express purpose of determining which, if either, of these two leads was the more helpful clinically.

METHODS

Leads IV R and IV F were obtained together with the three conventional leads in 400 electrocardiographic examinations of 349 subjects. Selection was exercised only in the sense that the precordial leads were taken in cases of known or suspected heart disease. In all instances the electrocardiographic examination was merely incidental to a complete clinical study, and the great majority of the patients were hospitalized.

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Two standard laboratory models of string galvanometer electrocardiographs* were employed. For the conventional leads and the indifferent (distant) contact of the precordial leads German-silver-plated electrodes, 4 by 6 cm. in size, were strapped to the extremities. For the exploring (near) electrode of the precordial leads a grooved, silver-plated disc, 3 cm. in diameter, was held at the desired location either by an attendant or by the patient's left hand. A proprietary electrode jelly provided a contact medium by means of which skin resistance was kept below 1000 ohms in all but very few instances. Lead IV R was obtained by pairing the right arm lead with the precordial electrode applied, as recommended,[1] to the extreme outer border of the palpable apex beat, or in the fifth intercostal space just beyond the left border of cardiac dullness, or just outside the midclavicular line if percussion of the heart was unsatisfactory. For Lead IV F the left leg was paired with the precordial electrode again placed as above. The galvanometer string tension was adjusted in all instances so that a deflection of one centimeter in the finished record corresponded to a potential difference of one millivolt. In order to obtain "upright" electrocardiograms, the connections for Lead IV F were so made that relative positivity of the apical electrode was represented by an upward deflection in the finished curve. All records were taken with the patient reclining at an angle of about 45°. When, early in the study, dissimilar precordial electrocardiograms were obtained, the examination was often repeated to rule out error in connecting the patient; in all the instances here reported the repeated records were practically identical with the original set.

RESULTS

Among the 400 pairs of precordial electrocardiograms obtained there were sixty-four instances of significant discrepancy. For convenience in presenting the data, all of the essentially similar records were considered together, and the general characteristics of Leads IV R and IV F, as encountered in this group, are briefly presented below in Section I. The instances of dissimilar precordial electrocardiograms are separately analyzed later in Sections II and III.

SECTION I. ANALYSIS OF ESSENTIALLY SIMILAR LEADS IV R AND IV F

P Waves.—In Lead IV R the P wave was almost invariably present as an upright deflection 1 to 1.5 mm. in amplitude, and sufficiently well defined to permit ready measurement of the P-R interval. In a few records P was isoelectric, and in a few others it attained an amplitude of 2 and 2.5 mm., but in no case was it a negative deflection in this lead. In Lead IV F, on the other hand, the P wave was usually either absent (isoelectric), or was a very small, diphasic wave, too ill-defined to permit accurate measurement of the P-R interval. In approximately 5 per cent of the records, P appeared as a positive deflection 0.5 to 1.5 mm. in amplitude, and in about 12 per cent the P deflection was negative in direction and 0.5 to 1.5 mm. in depth. In no instance was the P wave in Lead IV F a larger positive or more clearly defined deflection than in Lead IV R. Lead IV R, therefore, appeared preferable to IV F for depiction of the auricular wave and A-V conduction.

*"Hindle" Electrocardiograph, Cambridge Instrument Co.

QRS Complexes.—The QRS complexes, though usually diphasic, showed a wide range of variation in direction, from totally positive to totally negative. This was not unexpected in a collection of normal and abnormal electrocardiograms taken almost indiscriminately among patients known to have or suspected of having heart disease. Of greater interest, from the standpoint of comparison of the two leads, was the observation that in practically 75 per cent of the tracings the QRS directions were essentially the same in both leads. In the remaining 25 per cent, QRS was a more positive complex in Lead IV F than in IV R in all but one instance; in this, the QRS was entirely positive in IV R and balanced in IV F. The amplitude of QRS was essentially the same in both Leads IV R and IV F in half of the records. In 35 per cent of the tracings, QRS was 2 to 20 mm. larger in Lead IV R, with an average preponderance of 6.5 mm. In the remaining 14 per cent of the records, QRS was 2 to 20 mm. larger in Lead IV F, with an average preponderance of 5 mm. for this small group. Considering all of the records, QRS averaged 1.5 mm. greater in Lead IV R than in Lead IV F. In summary, the QRS complexes of Leads IV R and IV F were similar in the majority of instances. Dissimilarity was manifested largely in a tendency for QRS in IV F to be more often a positively directed complex, but slightly smaller in amplitude than in IV R.

RS-T Features.—In approximately half of the records, the RS-T junction was one-half to several millimeters above the isoelectric line. Whether elevated, isoelectric, or low, the junction was essentially the same in both Leads IV R and IV F in 73 per cent of the records. In all of the remainder the junction was more positive in position in IV R by 0.5 to 2 mm., including four instances in which the junction occurred below the isoelectric line. In the majority of records (57 per cent) the T wave appeared to take off directly from the QRS complex. When a horizontal RS-T segment was present in one of the precordial leads it was invariably present in the other. In only slightly less than 10 per cent of all the tracings was the RS-T segment slightly longer in one lead than in the other, but when such a difference occurred it was seen approximately twice as often in Lead IV F as in IV R. In summary, the RS-T junction level was similar for Leads IV R and IV F in the great majority of instances, but in an appreciable number of records the junction was higher (more strongly positive) in Lead IV R than in IV F. Slightly less than half of the records showed a horizontal RS-T segment, but this was usually of about the same degree in both precordial leads.

T Waves.—In electrocardiograms in which the T wave was positive both in Leads IV R and IV F, it showed a definite tendency to be larger in Lead IV R. Thus, in 200 such pairs in which the T-wave amplitudes were carefully measured, 62 per cent of the records showed that T in Lead IV R exceeded that of Lead IV F by an average of 2.5 to 3 mm.,

and in individual cases the difference was occasionally 6 or 7 mm. In 37 per cent of this group, T was of the same positive amplitude in both precordial leads. Only twice did the amplitude of T in Lead IV F exceed that in IV R. When both Leads IV R and IV F possessed negative T waves, the depth of the inversion was equal in exactly half the records, but in the remainder, T was more deeply inverted in Lead IV R about three times as often as in Lead IV F. In summary, the T wave, whether positive or negative, tended to be a larger deflection in Lead IV R than in Lead IV F.

Q-T Duration.—Careful measurement of the Q-T duration in 115 unselected pairs of precordial leads yielded identical values after corrections were made for differences in heart rate. In this respect, therefore, Leads IV R and IV F appear to be identical.

SECTION II. COMPARISON OF DISSIMILAR LEADS IV R AND IV F, WITH PREDOMINANT ABNORMALITIES IN IV F

Sixty-four pairs of precordial leads exhibited greater discrepancies than those summarized in Section I. These dissimilarities concerned particularly the RS-T segments and T waves. In fifty-five of these records Lead IV F revealed abnormalities greater in degree and pathologic significance than were noted in IV R. This group is presented for convenience under several roughly etiologic subdivisions, as follows:

Coronary Thrombosis Group.—Eighteen patients with a diagnosis of coronary thrombosis had electrocardiograms in which Lead IV F gave clearer indication of the infarct than did Lead IV R. Samples of the precordial leads are given in Plates I and II, and the accompanying legends offer other electrocardiographic and clinical details.

In three patients with recent coronary thrombosis (Plate I, Figs. 1, 6, and 7), Lead IV R was entirely normal, while IV F was sufficiently abnormal to confirm the clinical diagnosis. It is to be noted, however, that in none of these records was the R wave lost, which is considered typical of thrombosis in the left coronary artery system,[2] nor were the standard leads typical of either anterior or posterior infarction. However, the outcome in the first case, and the clinical features and electrocardiographic developments in the other two, pointed to coronary thrombosis. The atypical electrocardiographic features may have resulted from an unusual location of the lesion.

All of the cases illustrated in Plate I, by Figs. 2, 3, 4, 5, 8, 11, and 12, presented earlier or more dramatic changes in Lead IV F than in IV R. In follow-up records on three of these patients the T-wave abnormalities developed more fully in Lead IV F, but failed to appear at all in Lead IV R (Plate I, Figs. 4, 6, and 7).

In five cases of coronary thrombosis which had occurred in the distant past, the lesion was more definitely revealed in Lead IV F than in IV R (Plate I, Figs. 8*a*, 9, 13, and 15; Plate II, Fig. 1). Particularly

interesting was the fact that, in a case in which changes typical of anterior and apical cardiac infarction had been portrayed equally well in both precordial leads until a month after the acute episode, Lead IV R had returned to normal four months later, whereas the T deflection was still negative in Lead IV F (Plate I, Figs. 14*a* and *b*).

Digitalis Group.—Nine of the patients who were under the influence of digitalis exhibited electrocardiograms in which the T deflection was positive in Lead IV R and negative in Lead IV F. Whether digitalis was the only, or chief, factor in the T-wave inversion is open to reasonable question, because hypertension was present in six of these subjects and, as will be seen below, negativity of T may occur in the precordial leads of such patients. However, the RS-T and T changes exhibited in Plate II, Figs. 4, 5, 7, 9, 10, and 11, are like those generally recognized in standard leads as of the "digitalis variety." Definite evidence that digitalis was a causative factor was found in subject J. B. (Plate II, Fig. 7). An electrocardiogram obtained one week prior to digitalization showed large, positive T waves in Lead IV F; following the administration of digitalis, T assumed the opposite direction here illustrated. Again, in subject J. T. (Plate II, Fig. 8), who had neither hypertension nor clinical evidence of coronary occlusion, but manifested digitalis intoxication with coupled rhythm, the fact that T was isoelectric in Lead IV F would appear to be explainable as an effect of digitalis.

Hypertension Group.—Hypertension of considerable degree or long duration has been known frequently to alter the direction of the T wave in the limb leads[3] and precordial leads.[4] Although inversion of the T wave in both of the precordial leads of patients with hypertension was commonly encountered in this study, there were eight subjects in whom the T deflection was positive in Lead IV R, but deeply inverted or, in two instances only, diphasic or isoelectric in Lead IV F. None of this group was receiving digitalis.

Miscellaneous Group.—Twelve instances of significant discrepancy between Leads IV R and IV F were encountered in five patients whose etiologic diagnoses differed from those considered above. Samples of their precordial electrocardiograms are illustrated in Plate III, Figs. 9 through 13, and the accompanying legends contain descriptive clinical notes. None of these subjects was receiving digitalis. It is remarkable that in only three of the many instances of arteriosclerotic heart disease uncomplicated by hypertension or coronary thrombosis included in this study were there significant differences between Leads IV R and IV F. They are depicted in Plate III, Figs. 11, 12, and 13.

The attempted etiologic grouping of the data in this section served chiefly the purpose of convenience. Some overlapping of cases in each category is readily acknowledged, and no deductions as to the respective value of these two precordial leads in relation to etiology should

PLATE I

Coronary Thrombosis Group.

Fig. 1.—G. S., male, 70 years old. Several long, severe attacks of coronary pain during week. No previous cardiac symptoms. *EKG:* Isoelectric T in Lead I, and deeply negative T in Lead IV F only. *Course:* Sudden death five days later in another severe attack.

Fig. 2.—D. A., female, 70 years old. Known to have had hypertension for five years. Sudden attack of cardiac asthma with fall in blood pressure, followed by progressive congestive failure with death ten weeks later. *EKG:* Prominent Q wave and negative T in Leads II and III; T positive in Lead IV R, but negative in IV F.

Fig. 3*a* and *b*.—N. F., male, 56 years old. Sudden, severe attack of typical coronary pain, with collapse, cyanosis, hypotension, and transient fever and leucocytosis. *EKG*, twenty-four hours after onset, showed only low voltage in Leads I, II, and III, with neither precordial lead typical of recent infarction (3*a*). Two days later standard leads still equivocal, but Lead IV F now typical (3*b*).

Fig. 4*a* and *b*.—I. B., female, 72 years of age. History of treated syphilis. Typical attack of coronary occlusion, with transient fever and leucocytosis. *EKG*, two days after onset, showed left axis deviation and negative T deflection in Leads I, II, and III; precordial leads indeterminate (not illustrated). Nine days later, T isoelectric in Lead IV F only (4*a*), and five days later T had become inverted in Lead IV F but not in IV R (4*b*).

Fig. 5*a* and *b*.—W. P., male, 42 years of age. Angina pectoris for five months. Unusually severe attack, ten days before admission, lasting four hours, accompanied by sweating, weakness, nausea, and fall in blood pressure; fever and leucocytosis transiently. *EKG*, ten days after onset, showed left axis deviation and "cove-plane" T-wave inversion in Lead I; Lead IV F far more typical of recent infarction than IV R (5*a*), but a week later both precordial leads equally abnormal (5*b*).

Fig. 6*a* and *b*.—L. E., female, 64 years old. Arteriosclerotic heart disease, with hypertension and moderate angina pectoris. Clinically typical acute coronary occlusion, with pericardial friction, fall in blood pressure, fever, leucocytosis. *EKG*, three days after onset, showed marked left axis deviation and diphasic T in Lead III; the latter became deeply negative six days later. Lead IV R normal throughout, but T in Lead IV F was probably abnormal in both records (6*a* and *b*). Tracing one week later identical with above.

Fig. 7*a* and *b*.—A. M., female, 73 years old. Serologic tests for syphilis were positive. Crushing chest pains with dyspnea and vomiting; transient fever and leucocytosis. *EKG*, two weeks after onset, showed low voltage, very low T waves in Leads I and II, normal Lead IV R, and a diphasic T in Lead IV F (7*a*). Eleven days later, T inverted in Lead I, isoelectric in Lead IV F, but Lead IV R still normal (7*b*).

Fig. 8*a*, *b*, and *c*.—J. P., female, 50 years of age. Known to have had hypertension with angina pectoris for three years. Typical left coronary artery thrombosis with classical serial electrocardiographic changes. Admitted to hospital because of chronic pyelitis. *EKG*, two years after known coronary thrombosis, showed marked left axis deviation and isoelectric T in Lead I. Precordial leads both abnormal, but IV F more characteristic of old infarct than IV R (8*a*). Six weeks later suffered another attack of coronary thrombosis. *EKG*, taken one and ten days after last episode, showed negative T in Lead I. Both precordial leads again markedly abnormal, but again Lead IV F showed greater changes (8*b* and *c*).

Fig. 9.—G. W., male, 60 years old. Alleged to have had a typical attack of coronary thrombosis at home eight months before; referred to laboratory for follow-up examination. *EKG:* Isoelectric T in Lead I, and negative T deflection in Lead IV F only.

Fig. 10.—R. F., female, 45 years old. Serologic tests for syphilis positive, acute rheumatic fever at 35, with recurrent congestive failure thereafter. Severe attacks of coronary pain for two weeks before admission. Physical signs of mitral and aortic stenosis. Transient fever and leucocytosis. *EKG:* Right axis deviation, and small, negative T deflections in Leads II and III. In Lead IV F the high RS-T segment level, negative T wave, and absence of the R wave were considered typical of recent myocardial infarction; Lead IV R less strikingly abnormal. *Course:* Temporary improvement, with recurrence of congestive failure and death two months later. *Necropsy:* Complete occlusion of anterior descending branch of left coronary artery, healed infarct at left apex, mitral and aortic rheumatic endocarditis with stenosis, pulmonary and splenic infarcts.

Fig. 11.—T. O., male, 52 years old. Exertional angina pectoris for two weeks, with a severe episode lasting four hours. *EKG*, four days later, showed isoelectric T in Lead I, and dissimilar precordial leads; the abnormalities in IV F seemed more clearly indicative of coronary thrombosis than those in IV R.

Fig. 12.—C. C., male, 49 years old. Clinically typical coronary thrombosis, with ensuing hypotension, leucocytosis, and pericardial friction. Progressive congestive failure led to death in one week. *EKG*, four days after onset, showed left axis deviation and negative T deflection in Lead I. Lead IV F much more strikingly typical of recent myocardial infarction than IV R.

(*Legends continued on top of page 722.*)

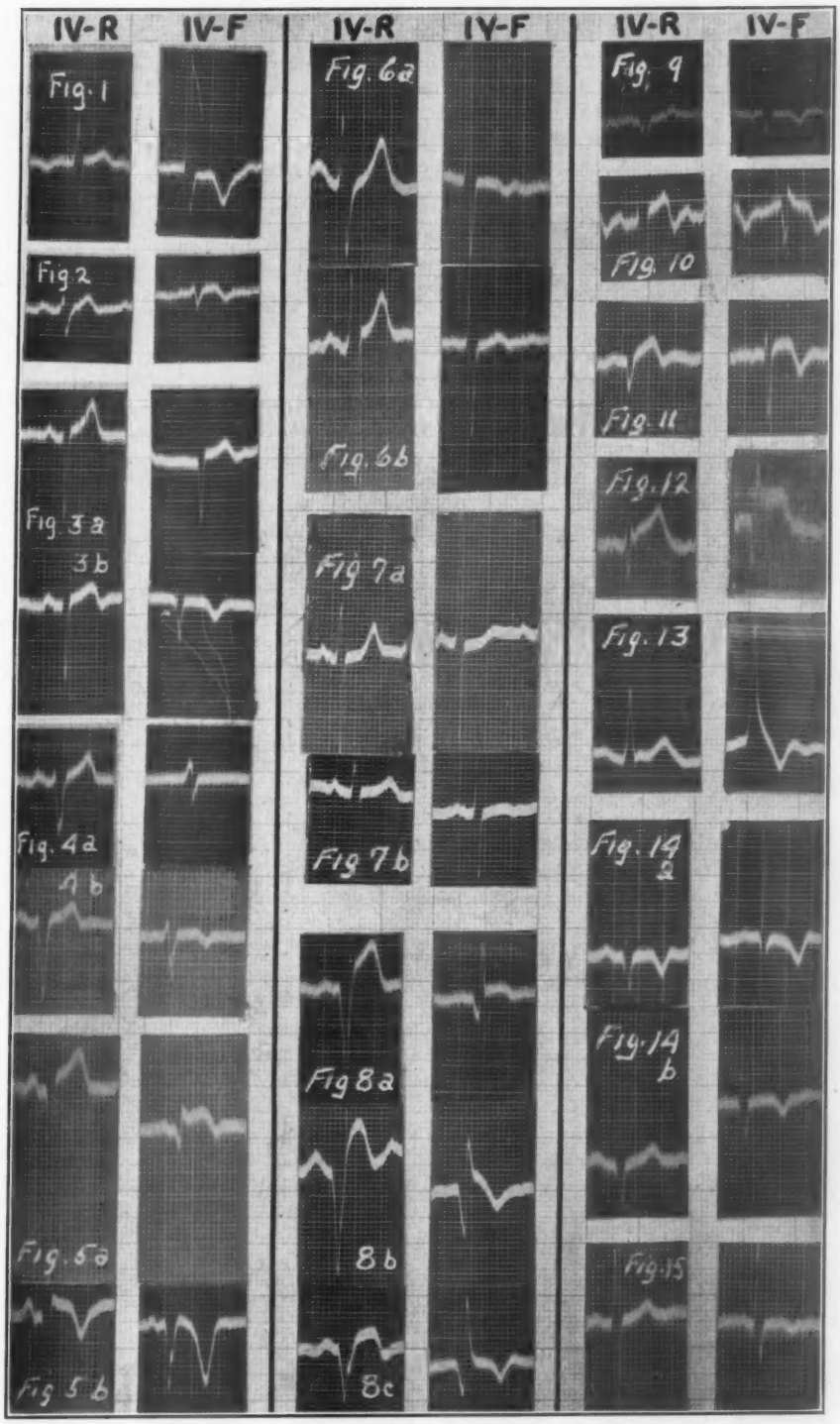

PLATE I

(See opposite page for legends.)

Fig. 13.—J. R., male, 60 years old. Hypertensive cardiovascular disease for twenty years. Apparently had coronary thrombosis eighteen months before admission, with angina pectoris thereafter. *EKG:* Incomplete A-V block, marked left axis deviation, and negative T deflections in Leads I and II. Precordial leads possibly distorted by artifact, but Lead IV R apparently normal, while in IV F the inversion of T is unmistakable.

Fig. 14*a* and *b*.—E. C., female, 67 years old. Arteriosclerotic heart disease with hypertension. Coronary thrombosis with electrocardiographic indications of anterior and apical infarction. *EKG,* one month after acute episode, showed persistent inversion of T in Leads I and II and both precordial leads (14*a*). Four months later, Lead IV R restored apparently to normal, while Lead IV F retained negative T deflection (14*b*).

Fig. 15.—J. C., male, 77 years old. Coronary thrombosis two years before, with typical electrocardiographic signs of apical and anterior infarction; angina pectoris subsequently. *EKG,* two years after acute episode, showed left axis deviation and diphasic T in Lead I. Lead IV R normal, while IV F still had negative T deflection.

PLATE II

Coronary Thrombosis Group (cont.)

Fig. 1.—J. C., female, 64 years old. Hypertension, and, probably, coronary thrombosis ten months before she was admitted to hospital for carcinoma of pleura. No evidence of pericardial metastases. *EKG* showed low voltage in standard leads, with small, positive T deflections. Of the precordial leads, only IV F showed a persistently abnormal T deflection.

Fig. 2*a* and *b*.—A. B., negro male, 54 years old. Severe angina pectoris for two years, with virtual invalidism. *EKG* showed shallow inversion of T in Leads II, III, and IV F, but not in IV R. Another tracing, three days later, taken to exclude possibility of technical error in obtaining the precordial leads, was identical with the first (2*b*).

Fig. 3*a* and *b*.—A. N., male, 67 years old. Arteriosclerotic heart disease, with hypertension and angina pectoris. Admitted for upper abdominal pain and chills. Roentgenograms disclosed filling defect in ascending colon, and displacement of kidney. Because of acute development of dyspnea, cyanosis, and pulmonary edema, patient was digitalized rapidly. *EKG:* Small T waves in Leads I and II. Lead IV R lacked an R wave, while Lead IV F showed deep inversion of T (3*a*). Two days later, T had turned downward in Lead IV R also (3*b*). *Course:* Sudden death one week later. Final diagnosis: questionable coronary thrombosis; carcinoma of colon.

Digitalis Group

Fig. 4.—W. V., male, 42 years old. Hypertensive heart disease and moderate congestive failure. Patient recently digitalized. *EKG:* Diphasic T wave in Leads II and III, and inversion of T in IV F but not in IV R.

Fig. 5*a* and *b*.—J. D., male, 51 years old. Arteriosclerotic heart disease with acute pulmonary edema. Digitalized, with prompt relief of symptoms. No hypertension. *EKG:* Typical digitalis-type T-wave inversion in Leads I and IV F, but not in IV R (5*a*). Tracing one month later showed similar, but less pronounced, abnormalities.

Fig. 6*a*, *b*, and *c*.—J. Q., male, 53 years of age. Arteriosclerotic heart disease with hypertension and moderate congestive failure. Patient fully digitalized. *EKG:* Three tracings in five days all showed left axis deviation and negative T deflections in Leads I and IV F only.

Fig. 7.—J. B., male, 58 years old. Arteriosclerotic heart disease with angina pectoris and mild congestive failure. Digitalized. *EKG:* Low voltage in standard leads, with almost isoelectric T in Lead I. T wave diphasic in Lead IV R, but definitely inverted in IV F.

Fig. 8.—I. A., female, 70 years old. Arteriosclerotic heart disease with hypertension and congestive failure. Digitalized. *EKG:* Auricular fibrillation, with isoelectric T waves in the standard leads and Lead IV F.

Fig. 9.—H. B., female, 32 years of age. "Malignant hypertension" with cardiac and renal failure led steadily to death in spite of digitalization. *EKG:* Left axis deviation. RS-T segment level slightly low in Lead I, but T waves positive in all leads except IV F, in which inversion of the digitalis type was present.

Fig. 10.—J. T., female, 74 years old. Arteriosclerotic heart disease with moderate congestive failure. Digitalis intoxication. *EKG:* Coupled rhythm, low T waves in Leads I and II. T was a positive deflection in Lead IV R, and negative in IV F. Note, also, opposite directions of T in the ectopic ventricular beats.

Fig. 11.—E. B., male, 58 years old. Arteriosclerotic heart disease, with hypertension and moderate congestive failure. Digitalized. *EKG:* left axis deviation, isoelectric T waves in Leads I, II, and III, and low RS-T segment level in Lead I. In Lead IV R the T wave was a positive deflection, while in Lead IV F it was negative.

Fig. 12.—F. B., male, 89 years old. Arteriosclerotic heart disease with hypertension and moderate congestive failure. Digitalized. *EKG:* Isoelectric T wave in Leads I, II, and IV F only.

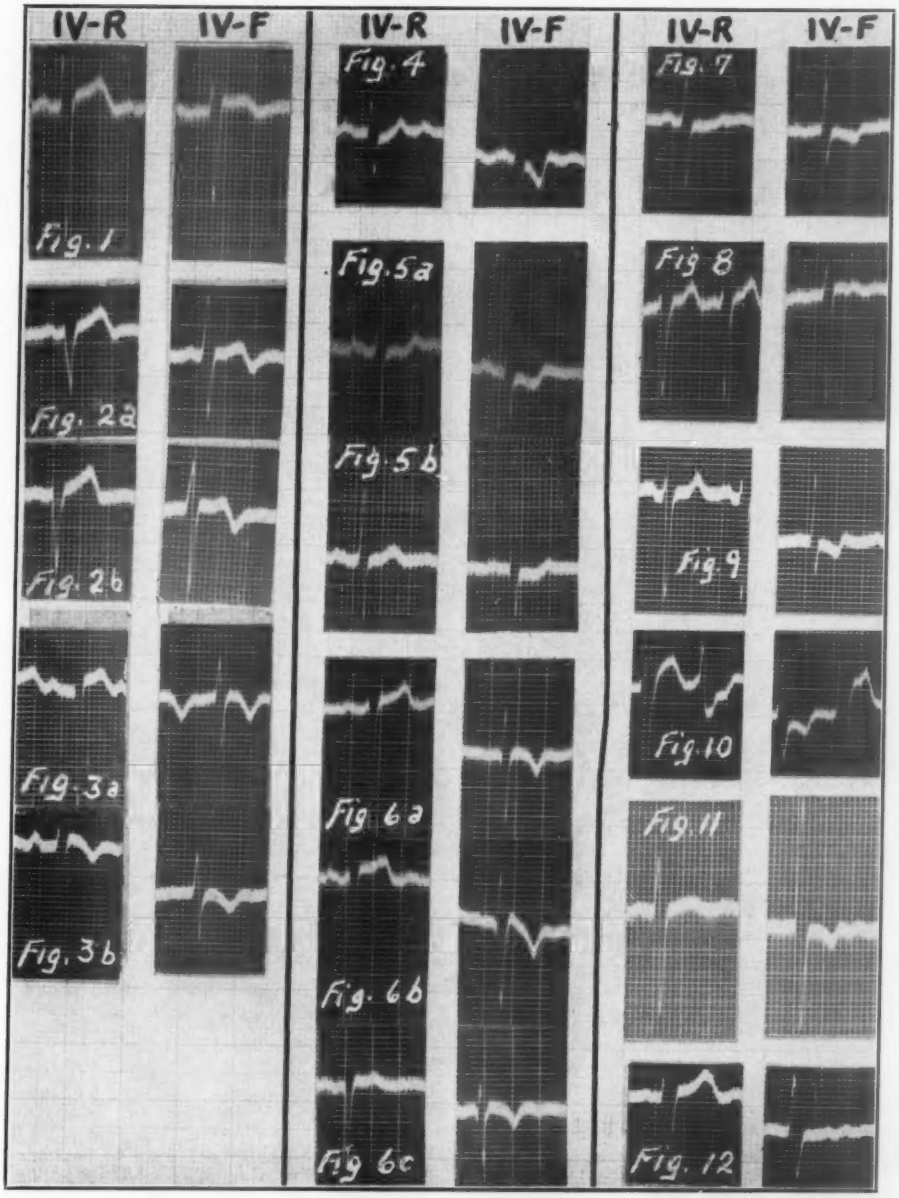

PLATE II

(See opposite page for legends.)

PLATE III

Hypertension Group

Fig. 1.—J. O., male, 40 years of age. Hypertensive cardiovascular disease, with subarachnoid hemorrhage. No digitalis. *EKG:* Marked left axis deviation, and negative T deflections in Leads I, II, and IV F, but not in IV R.

Fig. 2.—L. L., female, 51 years old. Severe hypertension, with mild congestive failure and cerebral symptoms. No digitalis. *EKG:* Marked left axis deviation, with negative T deflections in Leads I, II, and IV F; large positive T deflection in Lead IV R.

Fig. 3*a*, *b*, and *c*.—E. S., female, 61 years old. Arteriosclerotic heart disease and hypertension. *EKG:* Left axis deviation; negative T deflections in Leads I and IV F; large, positive T deflection in IV R (3*a*). Tracings repeated twice in week to rule out technical error, but records similar (3*b* and *c*).

Fig. 4.—J. T., female, 27 years old. Cushing's syndrome of pituitary basophilism, including hypertension. *EKG:* Left axis deviation, negative T deflection in Leads I and IV F only. Similar tracings eleven weeks later.

Fig. 5.—G. K., male, 85 years old. Arteriosclerosis and hypertension. No heart failure; patient not digitalized. *EKG:* Left axis deviation. T deflections in all leads, except IV F, were positive.

Fig. 6.—G. K., female, 54 years old. Hypertension and anxiety state. Possibly had coronary thrombosis eight months before. *EKG:* Marked left axis deviation, with negative T deflections in Leads I and II. Both precordial leads abnormal, but in IV R the T wave was isoelectric, while in IV F it was deeply inverted.

Fig. 7.—H. H., female, 40 years old. Obesity, with hypertension, and, probably, angina pectoris. No digitalis. *EKG:* Left axis deviation, diphasic T wave in Lead I. In Lead IV R the T wave was positive, while in IV F it was negative.

Fig. 8.—M. K., male, 75 years old. Arteriosclerotic heart disease with hypertension and congestive failure. *EKG:* Record obtained before digitalization showed normal T deflections in all leads except IV F. Following digitalization T became a negative deflection in all leads. *Course:* Congestive failure progressed in spite of digitalis and other treatment, and patient expired three weeks later.

Miscellaneous Group

Fig. 9.—C. L., male, 17 years old. Acute rheumatic pancarditis. No digitalis. *EKG:* T deflections small and inverted in Leads I, II, and IV F; T deflection small, but positive, in Lead IV R. In several other tracings taken during next three months the precordial leads remained much the same as those here illustrated; Lead IV R was always border-line with respect to the character of its T wave, while in IV F it was clearly abnormal in being consistently negative.

Fig. 10.—J. A., male, 58 years old. Arteriosclerotic heart disease with moderately severe angina pectoris. Digitalis discontinued three weeks before admission. *EKG:* T waves small, but upright in standard leads. Lead IV R perfectly normal, but in IV F the T deflection was deeply negative.

Fig. 11.—R. P., female, 72 years old. Arteriosclerotic heart disease, with, possibly, thiamin deficiency, and congestive failure. No digitalis. *EKG:* Left axis deviation, QRS slurring, and small, but positively directed, T waves in standard leads. T in Lead IV R appeared normal, while in IV F it was practically isoelectric. Five subsequent records in the course of several weeks were essentially the same, with persistent inconsistency in the precordial leads. *Course:* No clinical improvement with thiamin chloride administration, but recovery after digitalization.

Fig. 12.—C. R., male, 55 years of age. Rheumatic aortic stenosis, with syncopal attacks. No digitalis. *EKG:* Left axis deviation, with diphasic T waves in Leads I, II, and IV F, but a normal Lead IV R.

Fig. 13.—G. G., male, 54 years old. Arteriosclerotic heart disease with diabetes mellitus. No digitalis. *EKG:* Isoelectric T deflections in Leads I and IV R; however, in Lead IV F the T deflection was definitely negative.

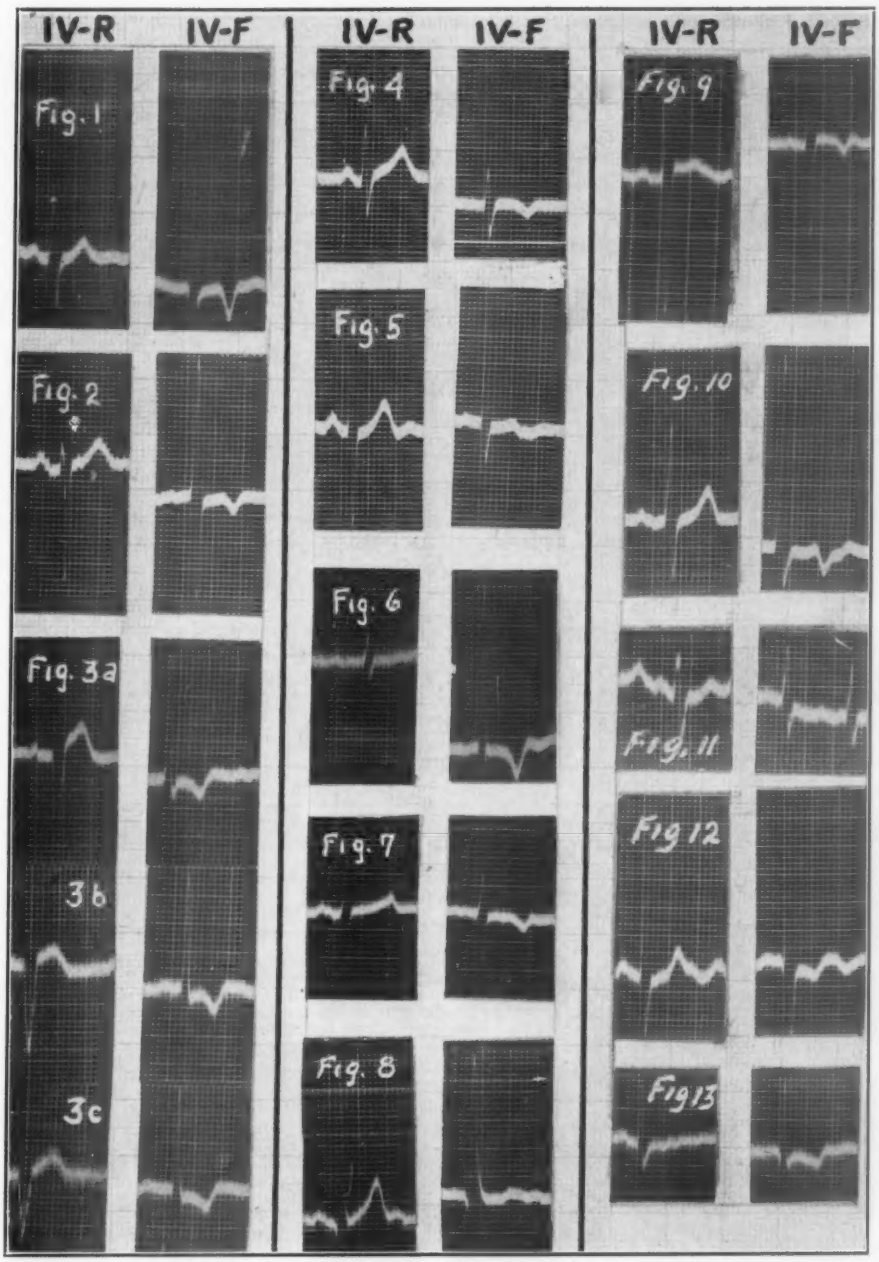

PLATE III

(See opposite page for legends.)

be ventured on so few data. The point that justifies emphasis is that Lead IV F may occasionally reveal significant abnormalities which are absent from, or less clearly presented in, Lead IV R.

SECTION III. PRESENTATION OF DISSIMILAR LEADS IV R AND IV F WITH PREDOMINANT ABNORMALITY IN LEAD IV R

In only nine instances (2.3 per cent), and from but four patients (1 per cent), were more definite abnormalities encountered in Lead IV R than in Lead IV F (Plate IV). In two of the patients coronary thrombosis had apparently occurred, and, although in both instances Lead IV F showed abnormalities of the T waves which might have confirmed the clinical impression, significant changes were more fully portrayed in Lead IV R of the earlier records (Figs. 1 and 2). Fig. 4 illustrates discrepancies in the precordial leads which were found in a case of probable vitamin B deficiency and cardiac failure. The T deflections were negative in Lead IV R, and positive in IV F. The greater abnormality of Lead IV R as compared with IV F, as shown in Fig. 3*a*, is of uncertain significance, and one cannot say in this case which lead gave more accurate information.

Apparently it is rare for Lead IV R to show greater abnormalities than Lead IV F, but even these few observations indicate that the possibility of such an occurrence must be recognized. However, discrepancies between these two precordial leads are revealed in the vast majority of instances (86 per cent) by greater abnormality in Lead IV F than in IV R.

PLATE IV

Fig. 1*a* and *b*.—A. S., male, 53 years old. Angina pectoris for eight years. Two recent, unusually severe and persistent attacks, associated with vomiting and collapse, followed by transient fever and leucocytosis. *EKG*, two days after onset (1*a*), indicated coronary thrombosis more clearly in Lead IV R than in IV F. Tracing fifteen days later showed abnormalities of equal degree in the two precordial leads (1*b*).

Fig. 2*a* and *b*.—R. H., male, 50 years old. Brief syncopal attack, followed by a questionable pericardial friction. *EKG*, two weeks later, suggestive of coronary thrombosis, with T-wave abnormality more fully developed in Lead IV R than in IV F (2*a*). Tracing six months later (2*b*) showed marked regression of T-wave abnormality in all leads, but QRS in Lead IV R more clearly indicative of old cardiac infarct. *Course:* Sudden death two weeks later.

Fig. 3*a* and *b*.—G. A., male, 61 years old. Acute epigastric and substernal pain, followed by obstructive jaundice and epigastric tenderness. Slight transient fever and leucocytosis: convalescence uneventful. *EKG:* two records in one week showed intraventricular block and changes of uncertain significance: Lead IV R in 3*a* more strikingly abnormal than IV F, but doubt about the diagnosis prevented any decision as to which lead gave more accurate information.

Fig. 4*a*, *b*, and *c*.—L. C., male, 52 years old. Arteriosclerotic heart disease with auricular fibrillation, and progressive congestive failure for eight months in spite of theoretically adequate digitalis medication. Diet considered deficient in vitamin B. Patient exhibited generalized anasarca and frank peripheral neuritis. Venous pressure 21 cm. water, arm-to-tongue circulation time 19 sec. Digitalis stopped because of marked bradycardia. Thiamin chloride and nicotinic acid given in large doses, mercurial diuretic given intravenously once; eliminated 15 pounds of edema fluid, and peripheral neuritis cleared up. *EKG:* Three records during first ten hospital days showing discrepancy in direction of T in precordial leads. Fourth record, three weeks later, not illustrated, showed positive T deflections in all leads. Final diagnosis: heart failure questionably related to vitamin B deficiency.

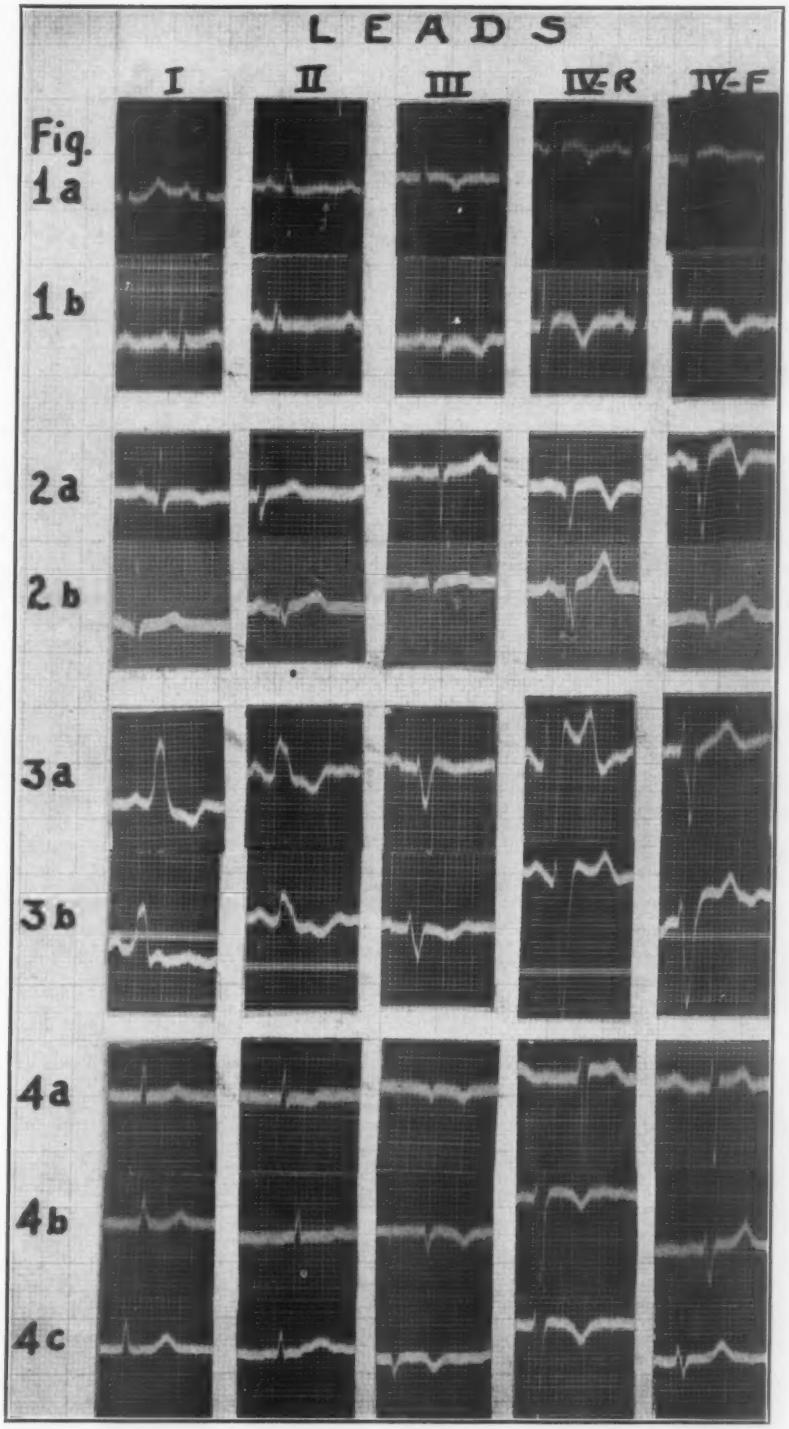

PLATE IV

(See opposite page for legends.)

SUMMARY

Leads IV R and IV F were studied in 400 electrocardiographic examinations of 349 patients known to have, or suspected of having, heart disease.

Although 84 per cent of the precordial leads were considered as being essentially the same, the following minor differences were noted in the two groups: Lead IV F was inferior to IV R in depicting the P wave and P-R interval. QRS in Lead IV F tended more often to be a positively directed complex, but was smaller in amplitude than in Lead IV R. The level of the RS-T junction was less often elevated (positive) in Lead IV F than in IV R. The T wave, whether positive or negative, was, on the average, smaller in amplitude in Lead IV F than in IV R. The Q-T duration was identical in the two leads.

Sixty-four pairs (16 per cent) of the records exhibited significant discrepancies, particularly in the RS-T portions and T waves. In fifty-five of these instances, the abnormalities occurred either alone in Lead IV F, or to a significantly greater degree in Lead IV F than in Lead IV R. Illustrations of all of the dissimilar precordial electrocardiograms are shown in the plates, and brief clinical notes are presented in the accompanying legends.

CONCLUSION

Lead IV F is definitely superior to IV R in the detection of cardiac abnormalities, and it should be given preference in routine clinical electrocardiographic examinations.

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ROENTGENKYMOGRAPHY OF THE HEART

Its Clinical Applications and Limitations

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THE application of roentgenologic methods to the study of the heart has proved an invaluable adjunct to clinical examination. Roentgenograms give a permanent record of the size, shape, and position, and under controlled conditions permit reasonably accurate measurements of the heart shadow. Fluoroscopy, by visualizing the movements of the heart, has afforded the opportunity to study its functional status, in addition to its morphologic variations. This method of examination gives information only to the individual observer, and its value depends upon the experience and skill of the one making the examination. The advent of roentgenkymography has provided a simple technique for graphically recording the movements of the heart on a single film. A permanent record of the motion is thereby obtained, which, upon closer inspection, reveals details of movements which are difficult or impossible to see with the poor illumination and speed of motion that obtain during fluoroscopic examination.

Increasing experience with this mode of study, considered in the light of the accumulated literature, now makes it possible to estimate its sphere of clinical usefulness as well as to recognize that it has certain definite limitations. The material for this report comprises the roentgenkymograms of 350 normal subjects of various ages, and those of a large number of patients with heart disease.‡ A list of selected references to the pertinent literature is appended.

The principle of roentgenkymography is very simple; it is illustrated in Fig. 1. If a lead shield with a thin horizontal slit is interposed between the subject and the sensitized film, the only part of the heart shadow registered on the film is the thin horizontal segment opposite the slit. If the film is moved downward during a continuous x-ray exposure, the pulsating movements of the two points visualized at corresponding levels on the two sides of the cardiac contour will be recorded

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‡The normal kymograms were taken in the diagnostic laboratory of the Equitable Life Assurance Society of the United States. The majority of the patients were studied at Kings County Hospital. The authors wish to acknowledge with thanks the cooperation of the x-ray department of Kings County Hospital, under the directorship of Dr. Richard Rendich; and are particularly obliged to Dr. Gilbert Alexander, who constructed the kymographic apparatus at Kings County Hospital and collaborated in the early phase of the study. Mr. Russell Stamm, of the x-ray laboratory of the Equitable Life Assurance Society, rendered valuable technical assistance.

on the moving film in the form of a wave, and the waves will be repeated with each cardiac cycle (Fig. 1).

This ingenious technique was first described by Sabat,[1] in 1911, but was almost entirely neglected for many years. The failing of the single-slit grid was that only two points of the cardiac contour were visualized. Stumpf[2] remedied this shortcoming and broadened the clinical applications of kymography by constructing a grid with multiple horizontal slits, making it possible to register numerous points along the cardiac contour simultaneously. With the multiple-slit grid the film must be moved only just a little less than the distance between two slits in order to prevent overlapping of the waves of adjacent segments. The type of grid most commonly employed has slits 0.4 mm. wide, spaced at 12 mm. intervals. The film is moved downward a little less than 12 mm. during a continuous exposure of one to two seconds, with respiration suspended in the phase of moderate inspiration. Thus, depending on the heart rate and duration of exposure, one to three complete cardiac cycles are generally recorded (Fig. 2). Since the film moves down during the exposure, the time ordinate is directed upward, i.e., the beginning of exposure is at the lower margin of a segment, the end of exposure above. For details of the technique the reader is referred to the articles of Hirsch.[3a, b]

The roentgenkymograph may be obtained commercially or can be built at relatively small expense.[4, 5] While the technique described is the one most generally employed, there are many variations. Thus, the grid may be moved and the film held stationary during the exposure, instead of moving the film as described above. The type of kymogram obtained with this method is illustrated in Fig. 3. Although the other thoracic structures appear in their normal configuration with this technique, the moving-film kymogram is usually preferable because it more closely portrays the movements of single points along the cardiac contour. Other types of grids have been employed. The grid devised by Cignolini[6] permits registration of a greater number of cardiac cycles than is possible with the multiple-slit grid, and therefore is preferable when a prolonged exposure is desired, as in the study of arrhythmias. In addition to the movements at the border which are recorded by the kymogram, there are density changes in the heart shadow during the cardiac cycle. These are usually visible grossly, but may be analyzed in greater detail with the densograph devised by Stumpf.[7]

The kymogram of a normal subject is illustrated in Fig. 2. The waves of each chamber are characteristic. The ventricular wave consists fundamentally of a slow, bent, outwardly directed limb representing diastolic filling, succeeded by a sharp inthrust representing systolic ejection. The peaks of the waves therefore represent maximum diastole, and the troughs represent maximum systole. By connecting the peaks and troughs of adjacent segments in the manner illustrated in Fig. 4, one can obtain the outline of the ventricle in systole and in diastole. The

aortic wave shows a sharp outthrust synchronous with ventricular systole, and this is succeeded by a slow recession of the wave during diastole, interrupted by the aortic incisura. The auricular waves consist of multiple small serrations.

All of the segments are comparable in time because all of them are taken during the same exposure. The waves of the different chambers, therefore, may be graphically correlated on a time axis, and the sequence of events throughout the cardiac cycle can be carefully analyzed. Fig. 5 shows a graphic analysis of the various waves on a time axis,

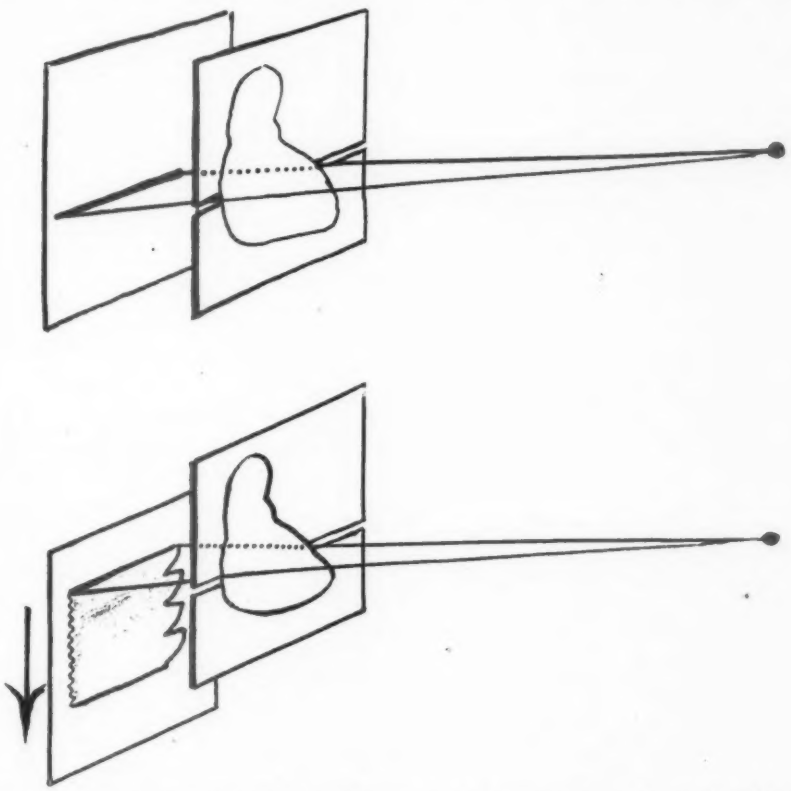


Fig. 1.—Principle of Slit Kymography. A lead shield with a thin, horizontal slit is interposed between the subject and the film, permitting only a narrow segment of the heart shadow, corresponding to the width of the slit, to be registered on the film. If the film is moved downward at a uniform rate during a continuous x-ray exposure, the pulsations of the two opposite points of the cardiac contour visualized will be recorded on the moving film in the form of waves, the waves being repeated with each cardiac cycle.

together with a simultaneously recorded electrocardiogram. By correlation with the electrocardiogram and heart sound records, the waves may be assigned to specific events in the cardiac cycle.[3, 8] The phenomena recorded kymographically are readily susceptible of physiologic interpretation. The ventricular wave corresponds roughly to experimental ventricular volume curves. The waves of the aorta and pulmonary artery are identical with arterial sphygmograms. The auricular

waves frequently show three small serrations which correspond to the a, c, and v waves of the jugular pulse.

An interesting application of kymography has been an attempt at topographical analysis of the chambers composing the borders of the cardiovascular silhouette. The infrequent occurrence of aortic waves over the upper right heart border indicates that the vena cava rather than the ascending aorta usually forms this part of the cardiovascular shadow. The presence of ventricular waves over the lower right border has suggested that the right ventricle enters into the formation of the right heart border, contrary to usual belief. While this is probably true of vertically placed hearts, there is a legitimate criticism against accepting the occurrence of ventricular waves over the lower right cardiac contour as indicative of right ventricular movement. The movements of the right heart border are probably appreciably influenced by the left ventricle. In general, the waves along the right heart border in the posteroanterior views are very variable and of little clinical importance. The auricular waves are of little value, for those produced by the right auricle are ordinarily too small to be of any practical significance, while the left auricle contributes only a small and inconstant segment to the left cardiac border in the posteroanterior view.

The left ventricular and vascular (aorta and pulmonary artery) waves are more constant, and undergo interesting modifications in disease. Changes occur in time relationships, form, and amplitude. The interpretation of changes in amplitude is less certain than analysis of time relationships, which may be accurately resolved within 0.02 to 0.03 second. Although Johnson[9] has found close correspondence between the amplitude of the left ventricular wave and the systolic output, the change in cardiac contour which the kymogram records is not purely a volume change, but is a resultant of the predominant contractile thrust, of rotary motion, and of positional changes of the heart as a whole. Furthermore, movement which is not parallel to the horizontal slit is distorted and magnified, as is evident in the upper ventricular frames of Fig 4. This distortion may, however, be easily corrected for in the manner illustrated.

The greatest objection to any quantitative interpretation of the kymographic waves is that, until now, kymograms have generally been taken at a distance of about 30 inches. Because of magnification of the image resulting from the short focal distance, no valid conclusions concerning heart size and its changes could be drawn. Teleoroentgenographic distance has not been attained hitherto because of the inability of ordinary Roentgen tubes to withstand the high exposure power required for kymography at the greater distance. Teleoroentgenographic distance has been made possible in our studies by the use of a tube of sufficiently high capacity, energized by a three-phase generator, which tends to maintain an almost even potential near peak value. One hundred eighty Ma. seconds at 60 to 85 kv., depending on the thickness of the chest and the

Fig. 2.

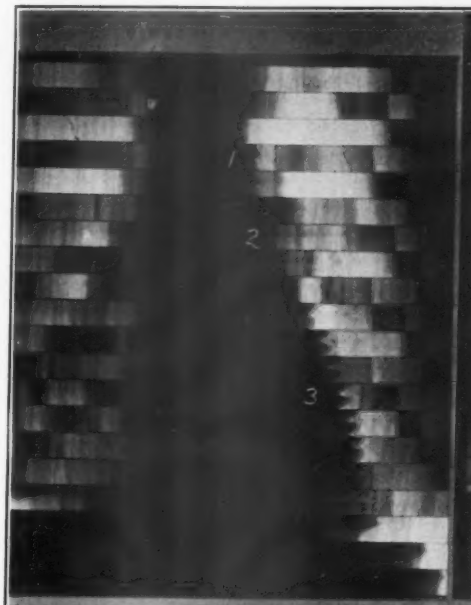


Fig. 3.

Fig. 4.

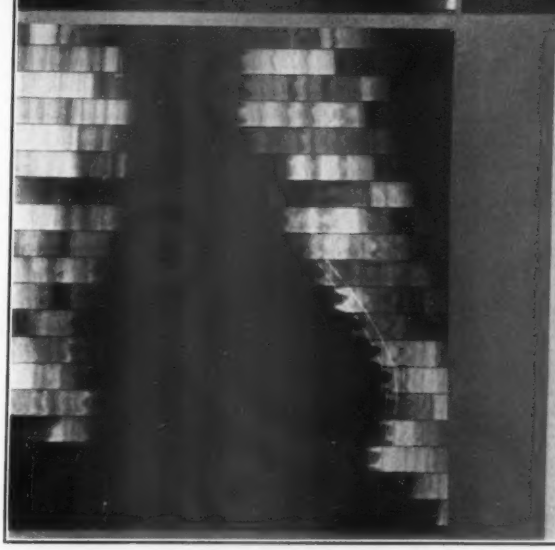


Fig. 5.

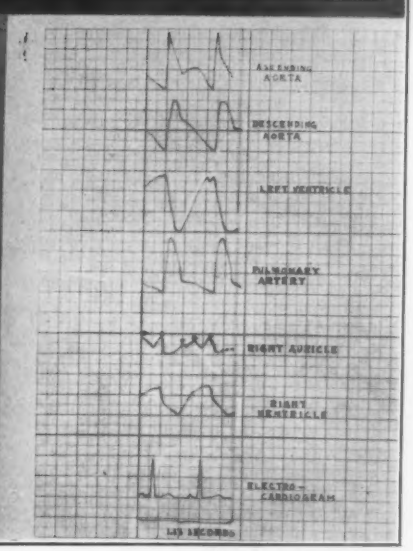


Fig. 2.—Roentgenkymogram of a normal subject.

Fig. 3.—Roentgenkymogram with moving grid and stationary film. The other thoracic structures appear in their normal relationships, in contrast to their segmented appearance in the moving film kymogram. This type of kymogram is not as satisfactory as the moving film kymogram, since it less accurately portrays the movement of single points of the heart.

Fig. 4.—Outline of the left ventricle in systole and in diastole. The peaks and troughs of each segment are projected to the same horizontal level before connecting them to obtain the outline of the ventricle in systole and in diastole. The kymogram records only that component of movement which is parallel to the slit, and the movement of the upper left ventricular contour is distorted and magnified because of the obliquity of this portion of the heart border. By connecting the peaks and troughs in the manner illustrated this factor is corrected, and the true amplitude of motion along the entire heart border is obtained.

Fig. 5.—Graphic correlation of the kymographic waves of various chambers in a normal subject, with a simultaneously recorded electrocardiogram. (Reprinted from Hirsch and Gubner, AM. HEART J. 12: 413, 1936.)

obliquity of exposure, were employed for a 1 to 1.5 second exposure. The measurements of the telekymogram correspond precisely to those of the regular teleoroentgenogram, and the telekymogram thus provides an accurate image of the heart and its movements. Telekymographic technique has been used by the authors in an attempt to obtain information concerning heart volume, cardiac output, and aortic elasticity.[10] For ordinary clinical purposes, however, when quantitative values are unnecessary, the 30-inch kymogram, which requires only ordinary equipment, serves adequately.*

MYOCARDIAL INFARCTS

The most important clinical application of kymography is in the demonstration of myocardial infarcts. Ordinary roentgenologic examination is of little value in myocardial disease except when it indicates cardiac enlargement, or when in an occasional case it demonstrates aneurysm of the left ventricle secondary to myocardial infarction. Although isolated case reports have appeared illustrating changes in contraction in areas of myocardial infarction,[11, 12] the value of kymographic examination in cases of coronary artery disease is not yet generally appreciated. In a study of forty-five cases of myocardial infarction the authors found definite kymographic changes in forty-one.[13] Exposures were made in the posteroanterior and in two left oblique positions (about 25° and 60°), thus visualizing the movements of the anterior and posterior walls of the left ventricle. A fairly close correspondence was found between the electrocardiographic and kymographic localization of the infarct in those cases in which electrocardiographic localization was possible. The kymogram was found to be valuable for localizing and determining the extent of infarction following acute coronary artery thrombosis. In addition, kymographic examination frequently aided in the appraisal of the extent of myocardial damage in patients with angina pectoris, and in subjects with a history suggestive of previous coronary thrombosis.

Infarcted areas appear in the kymogram as localized segments which exhibit abnormal pulsations. Most commonly, partial or complete paradoxical pulsation is observed. While the remainder of the ventricle contracts normally, the infarcted region expands passively, instead of contracting, at the onset of systole, and collapses at the end of systole. Other types of movement are also observed in myocardial infarction. A double systolic pulsation or multiple bizarre movements during systole may occasionally occur. Marked diminution of the amplitude of the ventricular wave may occur in other conditions, but a localized impairment of contraction with normal motion in adjacent segments is highly suggestive of myocardial disease. It is difficult to explain why in one case reversal occurs, whereas in another there is only impaired contraction;

*Teleoroentgenographic technique was employed for the films taken at the laboratory of the Equitable Life Assurance Society. The roentgenkymograms made at the Kings County Hospital were taken at 30-inch distance.

in fact, different abnormalities may be present in the same kymogram in neighboring segments. The variation is probably due in part to the extent of the lesion. Thinning of the myocardial scar following infarction, with a tendency toward formation of a ventricular aneurysm, would probably favor the development of paradoxical pulsation. On the other hand, lamination of an infarct by dense mural thrombi would probably result in absence of pulsation rather than reversal of movement.

These changes correspond closely to those observed by Tennant and Wiggers, with the myocardiograph, in experimental myocardial infarction.[14] They studied the effect of occluding branches of the dog's coronary arteries on the contractility of the area supplied. It was found that almost immediately after occluding a particular vessel the region supplied ceased to contract, and reverse movements took place. While the rest of the ventricle contracted normally, the ischemic area was distended during the period of heightened intraventricular pressure.

The type of kymogram commonly obtained in cases of infarction of the anterior wall of the left ventricle is illustrated in Fig. 6. There is complete reversal of pulsation over the lower half of the left ventricular contour. Posterior wall infarction may also be detected in the kymogram, although less frequently than anterior apical infarction, since even with oblique views the posterior wall of the left ventricle is not as fully visualized. Extensive areas of infarction involving both anterior and posterior walls may likewise be demonstrated kymographically by employing both posteroanterior and left oblique views.

The kymogram may occasionally be the means of demonstrating a ventricular infarct the existence of which is unsuspected clinically. Fig. 7 shows the kymogram in such a case. There is a definite reversal of movement of the lower half of the anterior wall of the left ventricle, with normal contraction in the oblique view. The patient was a man of 73 years, with a long-standing history of angina pectoris and impaired cardiac reserve. He gave no history suggesting coronary thrombosis. There was no cardiac enlargement. The electrocardiogram showed nothing indicative of myocardial infarction.

VENTRICULAR ANEURYSM

There is a striking disparity between the frequency with which ventricular aneurysm is encountered in post-mortem examinations and the rarity of cases in which the diagnosis is made during life. A diagnosis of ventricular aneurysm is usually made only when there is a definite bulge in the cardiac contour. Distension of the aneurysm is more marked in systole, when the intraventricular pressure is high, than it is in diastole, when there is practically no tension on the sac. Since diastole is considerably longer than systole at ordinary heart rates, roentgenographic exposures are more likely to record the heart outline in diastole than in systole. This may be one of the reasons why aneurysm

of the ventricle is not more commonly diagnosed by roentgenologic examination.

The systolic distention of ventricular aneurysms is illustrated clearly in Fig. 8 *B*, taken from a patient who had sustained several attacks of

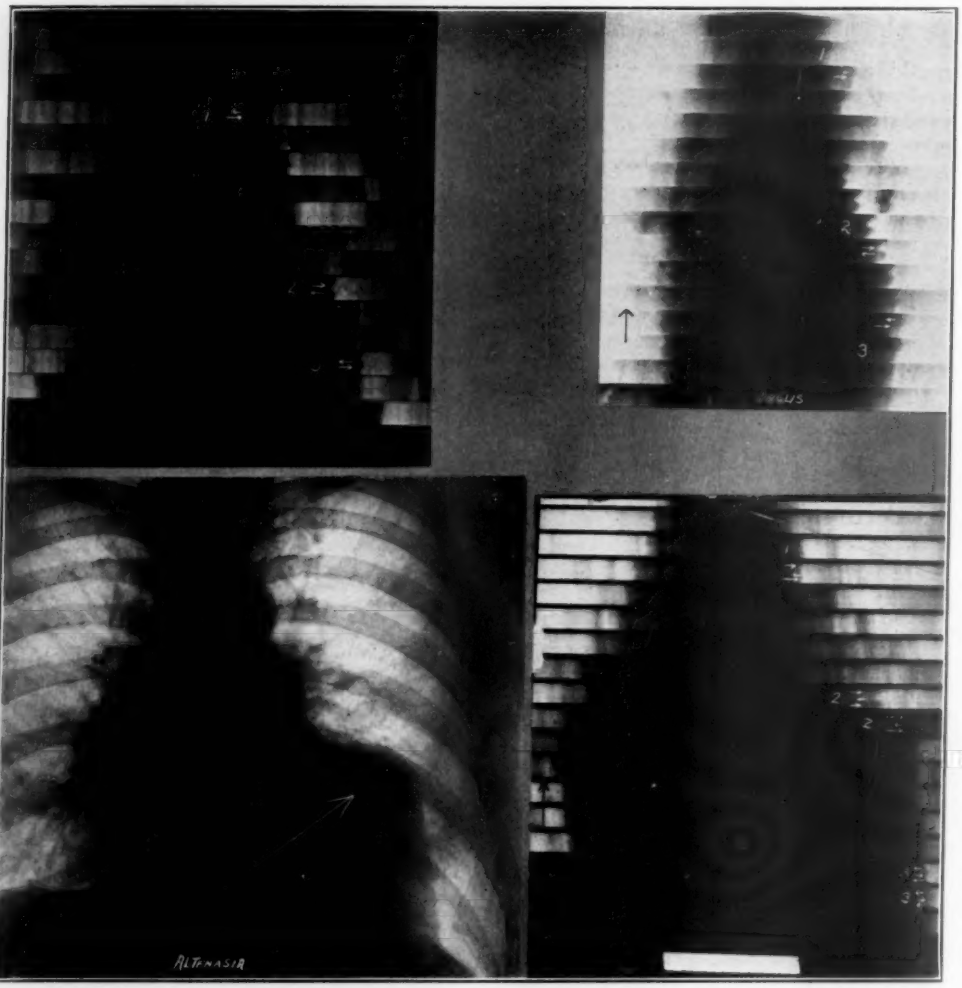


Fig. 6.

Fig. 7.

Fig. 8A.

Fig. 8B.

Fig. 6.—Myocardial Infarction. While the remainder of the ventricle contracts normally (*2*), the infarcted area (*3*) expands passively at the onset of systole instead of contracting, and collapses at the end of systole.

Fig. 7.—Roentgenkymogram of a patient with angina pectoris but without a history of coronary thrombosis and with a normal electrocardiogram. There is a definite reversal of pulsation of the apical and supra-apical region of the left ventricle, demonstrating an area of infarction.

Fig. 8.—*A*, Ventricular aneurysm. *B*, Roentgenkymogram shows systolic expansion of the aneurysmal sac, *2*.

coronary occlusion. During systole the aneurysm balloons out as a passive sac, just as the aorta expands, and collapses at the end of systole when the fall of intraventricular pressure relieves the tension on the aneurysmal area. Scott and Moore[15] have recently reported a case in which ordinary roentgenologic examination pointed to aneurysm of the ventricle, and the

kymogram showed paradoxical pulsation. At autopsy a highly malignant tumor, arising from the endothelium of the pericardium, was found. The underlying myocardium was invaded by the growth, and the destruction of the myocardium probably accounted for the paradoxical pulsation. We have observed the same roentgenographic and kymographic phenomena in a 13-year-old negress.

CARDIAC DECOMPENSATION

Marked enlargement of the heart, with cardiac decompensation, is generally accompanied by diminished amplitude of the ventricular pulsations, except in the case of aortic regurgitation. The movement of the apex is particularly reduced and may be absent or even reversed. This is due to impaired contraction of the ventricle as a whole, and to diminution or loss of the normal, upward, apical thrust. Furthermore, as Kirch[16] has emphasized, the apex is the most labile portion of the ventricle; atrophy and thinning of the apex, with consequent loss of contractility, occur whenever there is cardiac enlargement with failure, regardless of the cause of the failure. Impaired, absent, and even reverse, movement in the apical region must therefore be interpreted with great caution, in so far as the possibility of localized myocardial disease is concerned, when there is any considerable degree of cardiac enlargement.[17]

PERICARDIAL EFFUSION

The movements are markedly diminished, or almost absent, over the entire heart border in cases of pericardial effusion (Fig. 9 *A*). On occasion, from the kymogram alone, it may be difficult to distinguish pericardial effusion from the markedly diminished pulsations seen in cardiac decompensation with marked enlargement of the heart. After resorption or paracentesis, the amplitude of the ventricular wave tends to return to normal (Fig. 9 *B*).

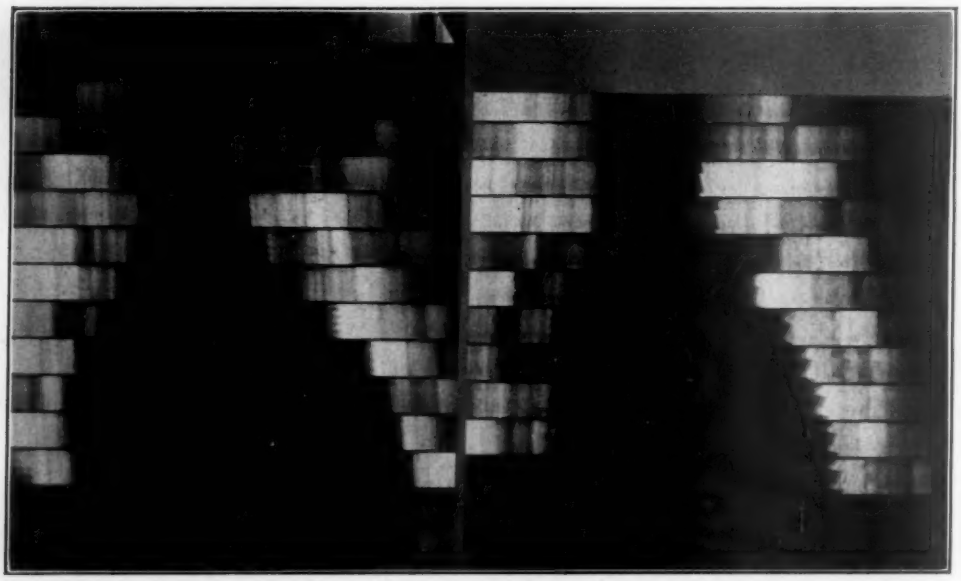
CONSTRICTIVE PERICARDITIS

Although the interpretation of diminution or absence of movement in cases of cardiac enlargement must be cautious, a generalized absence of movement when the heart is not enlarged is characteristic of concretio cordis, in which case the excursions are limited by the constricting pericardium. Fig. 10 illustrates a case of constrictive pericarditis in which the kymogram aided in the diagnosis. A pericardiectomy was performed, with complete relief of symptoms. Johnson[4] reported a similar case and stressed the diagnostic value of roentgenkymography in this condition.

VALVULAR LESIONS

Characteristic changes in the ventricular and vascular waves may occur when valvular lesions are present. These have been reported in detail elsewhere.[8]

In *mitral insufficiency* the pressure in the left auricle is increased markedly during ventricular systole because of the regurgitation. The rate of inflow into the ventricle in early diastole is accordingly accelerated, and there is practically complete filling in the early inflow phase. Under these circumstances the ventricular wave may assume a trapezoid appearance. Occasionally, when the regurgitation is marked,



A. *B.*

Fig. 9.—Pericardial Effusion: *A*, Roentgenkymogram shows generalized diminution of pulsation. *B*, Roentgenkymogram of same subject one month later, showing return of normal pulsations with resorption of the effusion. Reproduced through kind permission of Dr. Marcy Sussman, Roentgenologist of the Mount Sinai Hospital, New York City.

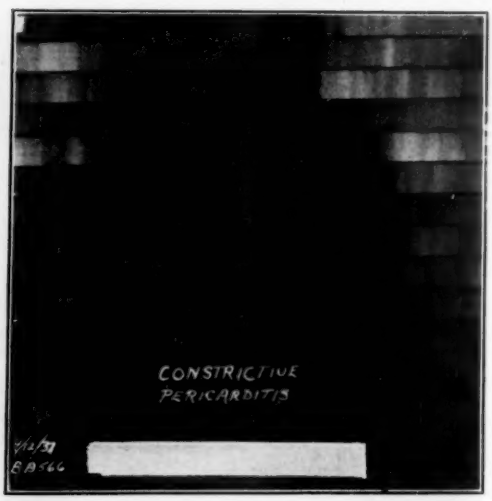


Fig. 10.—Constrictive pericarditis. There is a marked generalized impairment of contraction; heart of normal size.

a definite regurgitant wave may be seen in the auricle. Fig. 11 *B* shows filling of the auricle at the onset of systole in a case of advanced mitral valvular disease in which the enlarged left auricle formed the right heart border (Fig. 11 *A*).

In *mitral stenosis* the ventricular wave may be of low amplitude, and when the degree of stenosis is marked the filling of the ventricle in diastole is retarded, which is in contrast to mitral insufficiency.

Fig. 11*A*.

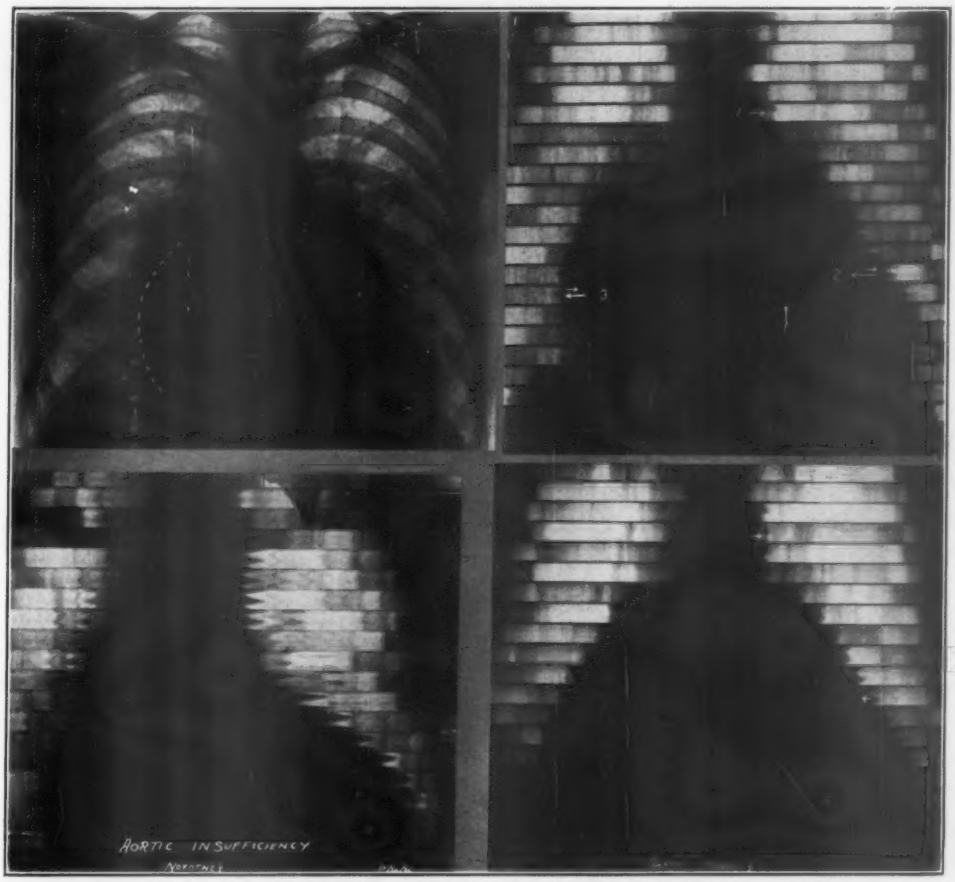


Fig. 11*B*.

Fig. 12.

Fig. 13.

Fig. 11.—Mitral Insufficiency: *A*, The enlarged left auricle forms the right heart border. *B*, Roentgenkymogram shows regurgitation into the left auricle, with onset of systole and a rapid refilling of the left ventricle in early diastole.

Fig. 12.—Aortic Insufficiency. The aortic waves are of large amplitude and collapsing character. The ventricular waves are large, indicating an increased systolic ejection; and there is a rapid refilling in early diastole due to the regurgitation.

Fig. 13.—Aortic Stenosis. The aorta fills slowly during systole.

Aortic insufficiency produces striking changes in the kymogram (Fig. 12). The amplitude of the aortic wave is greatly increased, to a degree commensurate with the widened pulse pressure, and collapses early in diastole. The ventricular wave is likewise of large amplitude because of the increased ejection, and refills early in diastole as a result of the regurgitation.

In *aortic stenosis* the aorta fills very slowly because of the diminished rate of ejection from the ventricle. This change occurs only when there is a marked degree of stenosis (Fig. 13).

In general, kymography is not of great clinical value in valvular disease. There is considerable variation among normal subjects in the appearance of the ventricular waves, which may resemble those seen in mitral insufficiency or stenosis. Characteristic changes are generally produced only when the lesion is advanced. Furthermore, valvular lesions are usually multiple, and the kymographic waves are a resultant of the combined dynamic effect of these lesions. Thus, the aorta may fill slowly in cases of mitral insufficiency because of the diminished rate of ejection from the ventricle, since pressure is dissipated by regurgitation into the auricle; this may simulate the slow aortic filling in aortic stenosis.

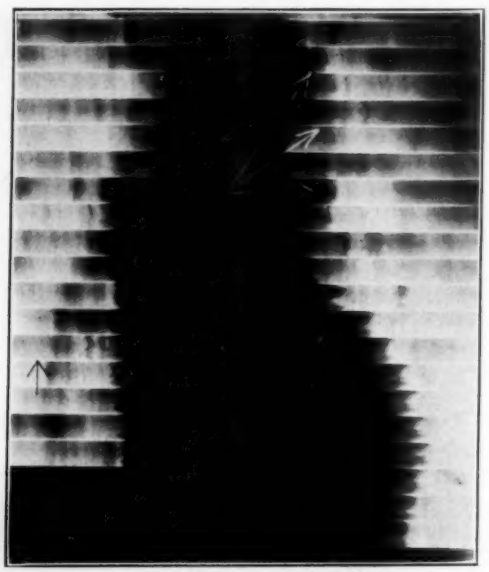


Fig. 14.—Aneurysm of the aorta.

DISEASES OF THE AORTA

Aneurysm.—It is frequently difficult to distinguish aortic aneurysms from mediastinal tumors, and kymography may help to identify the mediastinal mass. In general, aneurysms pulsate (Fig. 14), whereas solid tumors do not, but this statement requires many qualifications. Solid tumors situated in close proximity to the aorta may show transmitted movements which may be difficult to distinguish from the pulsations of the aorta. A helpful detail, when it is present, is the occurrence of cyclic density changes in aneurysm, in addition to movement at the border. An increased opacity of the mass which occurs at the same time as a lateral movement at the margin signifies movement in three dimensions, and indicates that the mass is expansile. Stumpf[7] has devised a

densograph to aid in detecting variations in opacity. It is important to recognize that aneurysms may fail to pulsate if clotting has occurred in the sac. Fig. 15 illustrates a case of this type. A densely laminated aneurysm of the ascending aorta and innominate artery was found at autopsy. Scott and Moore[15] have had similar experience. Blakemore and King[18] demonstrated a marked reduction of pulsation following electrothermic coagulation of aortic aneurysms and found that "roentgenkymography has been of great help in showing the effect of induced clotting on the pulsation of aneurysm."

Syphilitic Aortitis.—The signs of aortitis are few, and any definite change in movement detectable in the kymogram would have definite clinical value. Unfortunately, syphilitic aortitis most often involves the ascending aorta, the first part of which is obscured by the heart shadow, and kymographic movements of the remainder of this segment of the aorta vary considerably because they are influenced by the motion of the heart, which is in close proximity. Scott, Moore, and McCordock[19] stated that "the presence of large waves over the ascending aorta in adults below forty is most suggestive of syphilitic aortitis, and may be considered as such kymographically." In the posteroanterior view, the right side of the vascular shadow is formed by the superior vena cava, rather than the ascending aorta, in the majority of cases,[8] unless the aorta is definitely widened. While it is true that bizarre waves, which may even resemble ventricular waves, may be seen over the right border of the vascular pedicle, these cannot be accepted as characteristic of syphilitic aortitis, for they are observed in normal individuals during expiration,[20] and in other pathologic conditions. It is also questionable whether they represent expansile movements of the aorta. The ascending aorta and aortic arch are best visualized in the slight left oblique position. In this view it is seen that there is considerable variation in the appearance of the wave of the ascending aorta in normal subjects. It will be necessary to establish normal standards in this position before any changes characteristic of aortitis can be distinguished.

Arteriosclerosis.—Arteriosclerosis decreases the elasticity of the aorta. The velocity of the pulse wave is a quantitative expression of arterial elasticity, the velocity increasing with decreased elasticity. An attempt has been made with the telekymogram to estimate pulse wave velocity, and thereby elasticity of the aorta, by employing Bramwell's formula relating change in arterial cross section to pulse pressure.[10] With this method, normal values for pulse wave velocity in the descending aorta were estimated to be of a magnitude of 3 to 4 meters per second. Decreased arterial elasticity is frequently grossly distinguishable in the kymogram by the fact that the amplitude of the wave of the descending aorta is small although there are a normal or increased pulse pressure and a ventricular wave of normal magnitude. When calcific plaques are present in the aorta they may be seen to pulsate slightly.

The changes are usually more definite in the descending than in the ascending aorta, for arteriosclerosis more commonly involves the descending than the ascending portion. Furthermore, interpretation of movement of the ascending aorta is difficult because, in addition to its intrinsic expansile movement, there are probably an appreciable displacement of the ascending aorta by motion transmitted from the ventricles, and straightening of the aorta with increase in internal pressure (Bourdon action).

In hypertension the aortic wave may be of rather low amplitude. Since the aorta is already distended by a high diastolic pressure, its expansion in systole is consequently limited, and the kymographic wave of the descending aorta may appear rather small. The ventricular wave, however, is of normal or slightly increased amplitude, unless there is complicating myocardial damage.

DISEASES OF THE PULMONARY ARTERY

The waves of the pulmonary artery resemble those of the aorta closely; they are characterized by a rapid systolic outthrust succeeded by a gradual retraction, and the latter is interrupted by a prominent incisura. The diastolic collapse is somewhat more rapid than in the aorta. When the pulmonary artery shadow is increased in size as a result of disease the kymographic waves may vary, depending on the cause.

Patency of the ductus arteriosus (Fig. 16) causes waves of large amplitude in the pulmonary artery, reflecting an increased pulse pressure in the pulmonary circuit. This may be seen to extend to the larger branches in the hilar region. This phenomenon is known fluoroscopically as the "hilar dance."

With enlargement of the pulmonary conus secondary to mitral valvular disease the waves are of smaller amplitude than when the ductus arteriosus is patent, for the pulmonary artery is distended by a heightened diastolic pressure and its expansion is consequently limited (Fig. 17).

Aneurysm of the pulmonary artery is a rare lesion which is demonstrated well by kymography. Prominent arterial pulsations are present over the aneurysmal area (Fig. 18). In another case of pulmonary artery aneurysm recently observed by one of us, in which the diagnosis was confirmed at autopsy, there were also large pulsations. The small amplitude of the pulsations in the case of pulmonary artery aneurysm recently reported by Brown, McCarthy, and Fine[21] may have been due to clotting within the sac.

ARRHYTHMIAS

Multiple-slit kymography is not well suited for the study of arrhythmias because of the short exposure usually employed. The type of grid devised by Cignolini[6] permits a prolonged exposure and is better for this purpose, although at best roentgenkymography gives much less informa-

tion than electrocardiography with respect to the arrhythmias. The heart rate and time of onset and duration of systole and diastole may be accurately determined with the multiple-slit grid. Fig. 19 illustrates a case of heart block. The ventricular waves are of unusually large amplitude, indicating an increased systolic discharge resulting from the slow ventricular rate. Multiple, prominent, auricular waves are present over

Fig. 15*A*.

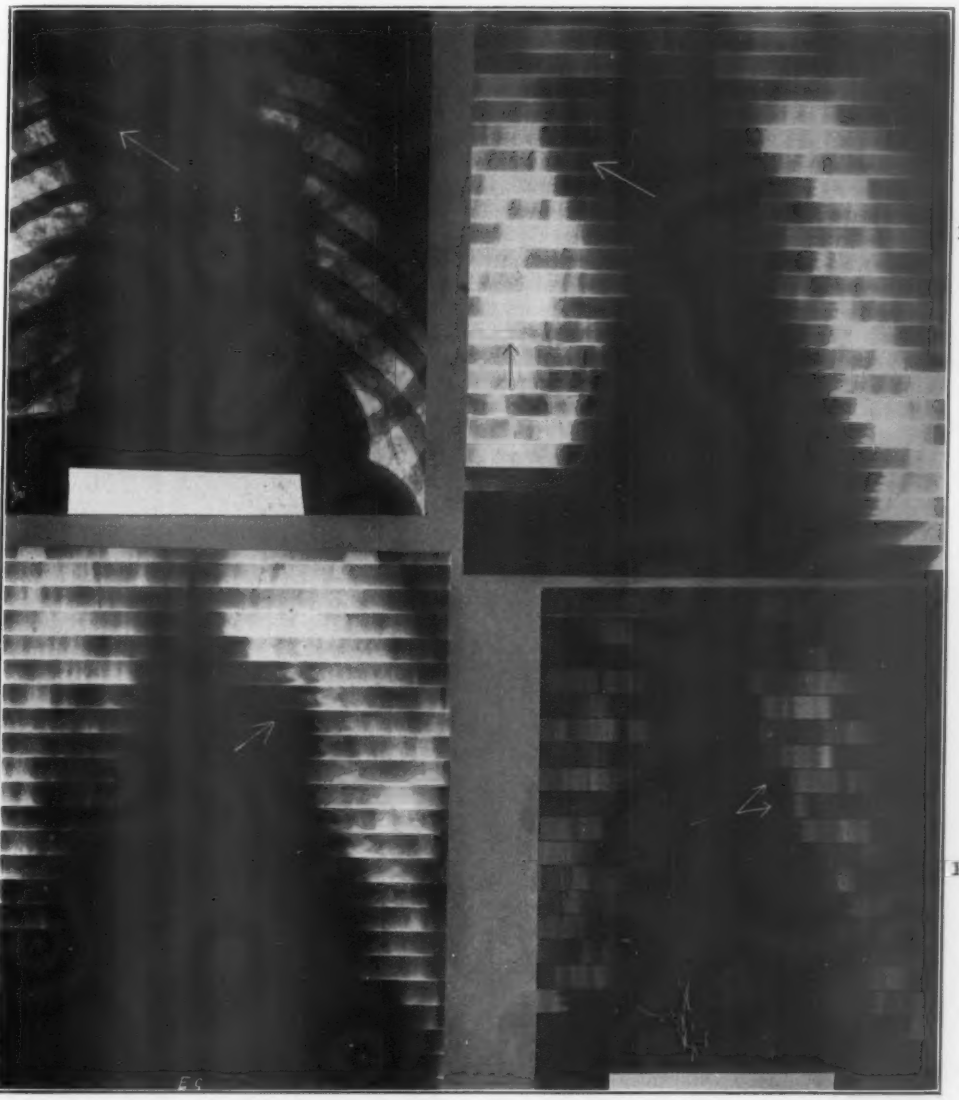


Fig. 15*B*.

Fig. 16.

Fig. 17.

Fig. 15.—*A*, Aneurysm of the aorta and innominate artery. *B*, Roentgenkymogram shows no pulsations of the aneurysm. At autopsy the aneurysm was found to be densely laminated with mural thrombi.

Fig. 16.—Patent ductus arteriosus. The pulmonary artery pulsations are of increased amplitude.

Fig. 17.—Mitral valvular disease. The pulmonic conus is prominent but the pulsations are of lower amplitude than when the ductus arteriosus is patent.

the right heart border. Fig. 20 illustrates an extrasystole, which is of smaller amplitude than the regular beat.

Wolferth and Margolies[22] demonstrated asynchronism in the onset of ejection from the two ventricles in bundle branch block by comparing the time of outthrust of the aortic and pulmonary arterial waves. Slight asynchronism between the two ventricles, of lesser degree, may occur normally.[23] A double peak in the ventricular wave has also been described in bundle branch block.[24] Some caution must be exercised in interpreting the ventricular waves in bundle branch block, since in these cases the heart is usually enlarged and the seat of considerable myocardial damage, which of itself may significantly alter the ventricular waves.

Fig. 18A.

Fig. 18B.

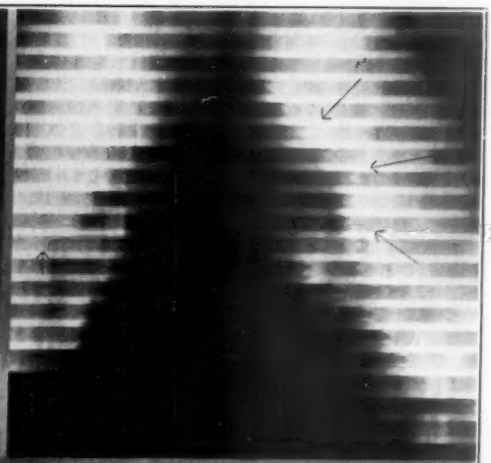


Fig. 19.

Fig. 20.

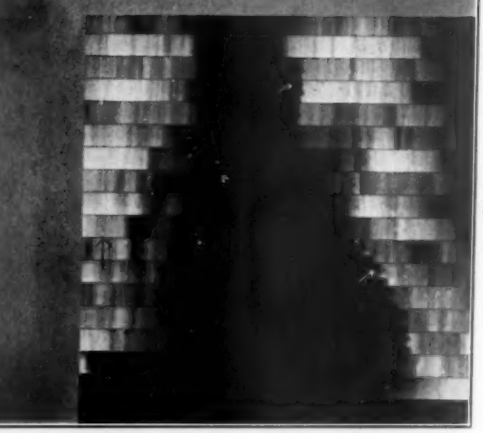


Fig. 18.—*A*, Aneurysm of pulmonary artery. *B*, Roentgenkymogram shows prominent pulsations.

Fig. 19.—Heart block. The ventricular wave is of large amplitude, indicating increased systolic ejection caused by the slow rate.

Fig. 20.—Extrasystole. The extrasystole is premature and of smaller amplitude than the preceding normal contraction.

SUMMARY

Roentgenkymography is a simple method of graphically recording the movements of the heart and great vessels, permitting an accurate and detailed analysis of the sequence of events throughout the cardiac cycle. The record is obtained on a single film with a short exposure of 1.5 seconds and entails no discomfort or hazard to the subject. The pulsations of the heart are recorded in the form of waves. The waves of the aorta and pulmonary artery correspond to arterial sphygmograms, while the ventricular waves resemble experimental ventricular volume curves.

In the interpretation of roentgenkymograms normal variations and certain important technical and physiologic factors must be considered before pathologic significance is attributed to changes which may be present.

The waves undergo changes of diagnostic significance in various pathologic states. The most important clinical application of kymography is in the detection of myocardial infarcts. Kymography may also be helpful in the diagnosis of constrictive pericarditis, pericardial effusion, and diseases of the pulmonary artery, and in distinguishing pulsating from nonpulsating tumors of the mediastinum. It is of little value in cases of valvular lesions except aortic insufficiency, in which characteristic changes occur.

While the method has limited clinical usefulness apart from these applications, there are other reasons why it is valuable. It provides a direct and convenient method for studying and teaching certain aspects of human cardiac physiology which have hitherto required difficult animal preparations employing the myocardiograph and arterial sphygmograph. In corroborating impressions of heart movement obtained by means of fluoroscopy it has given confidence to the radioscopist which is obtainable in no other fashion. It thus fills a definite need in the teaching field and should prove a most useful adjunct to fluoroscopic examination.

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CORONARY EMBOLISM

Report of Three Cases

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CORONARY embolism was described by Virchow[1] as early as 1856, but an exhaustive review of the literature, made by Saphir[2] in 1933, indicates that it is not a common condition, for he was able to find only eleven cases in which the diagnosis was satisfactorily proved. To these he added three of his own. The rarity of this disease has been variously attributed to the difference between the caliber of the aorta and that of the coronary arteries;[3] the situation of the coronary vessels at the root of the aorta; the right angle of emergence of the coronary arteries; the bulk and swiftness of the blood current in this portion of the aorta;[4] and the fact that the major part of coronary filling occurs in diastole.[2]

The emboli are usually detached portions of endocardial vegetations, fragments of arteriosclerotic plaques, or bits of disrupted mural thrombi, but they may consist of air, fat, tumor tissue, or inflammatory tissue. The left coronary artery, and especially its descending ramus, is the vessel which is most commonly obstructed. As death frequently ensues shortly after the occlusion, associated myocardial changes are not often found when the autopsy is performed. Because it is not always possible to identify an embolus by gross or microscopic examination of the occluded vessel, it is important to demonstrate a possible source for the embolus. Furthermore, the obstructed artery must be free from other disease which would be sufficient in itself to cause the occlusion. If these two criteria are fulfilled, the diagnosis can be established with reasonable certainty even in those cases in which the embolus has the structure of an ordinary thrombus.

The clinical diagnosis of coronary embolism is difficult because death is usually dramatically sudden. In those rare instances in which the course is more gradual, the possibility should be considered if there is evidence of coronary occlusion in the absence of coronary artery disease, and if a possible source for an embolus can be demonstrated.

In the past twenty years there have been three instances of coronary embolism among 12,300 consecutive autopsies performed at Cleveland City Hospital. These cases are of particular interest, in that death was more or less gradual, and myocardial infarction had developed in two instances.

Case 1.—J. B., a white man, 42 years of age, who entered Cleveland City Hospital June 14, 1938, complained of chills and fever. He had been in good health until one month previously, since which time he had had malaise, anorexia, weakness, diaphoresis, and daily chills and fever. There was no history of rheumatic fever.

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Examination showed that the patient was normally developed, but emaciated and seriously ill. The temperature was 39.2° C., and the pulse rate was 100 beats per minute. There were several petechiae over the trunk. The lungs were normal. Auscultation of the heart revealed a loud, blowing, systolic murmur, heard best at the apex. The blood pressure was 108/60.

The erythrocytes numbered 3,620,000 per cubic millimeter, and the hemoglobin was 55 per cent. The leucocyte count was normal. The urine was normal, and the blood Kline test for syphilis was negative. Fluoroscopic and roentgenographic studies of the chest showed that the heart was of normal size and shape.

During the patient's stay in the hospital the temperature varied between 36.7° C. and 40.5° C. On numerous occasions petechiae were present in the retinae and the skin. Nevertheless, twenty-three blood cultures were negative. Albumin, casts, leucocytes, and erythrocytes appeared in the urine. The hemoglobin fell to 38 per cent. Serial roentgenograms of the chest showed progressive enlargement of the heart; the transverse diameter increased from 13.2 cm. to 16.5 cm. The greatest internal diameter of the chest was 34 cm. At no time did the patient complain of pain in the chest. An electrocardiogram taken July 18 showed no abnormalities. He died August 17, on the one hundredth day after the onset of his illness. The clinical diagnosis was subacute bacterial endocarditis and acute focal glomerulonephritis.

Autopsy Findings.—(Autopsy No. A-12294, performed by Dr. T. C. Laipply, four hours after death.) The body was that of a normally developed but poorly nourished white man, approximately 47 years old. There was marked pallor of the skin and mucous membranes, and numerous petechiae and large ecchymoses were present in the skin and conjunctivae. The pericardial sac contained 25 c.c. of cloudy, amber fluid, and the lining surface was dull, gray, and covered by flecks of fibrin.

The heart weighed 450 gm. All of the chambers were dilated. The wall of the right ventricle measured 4 mm. in thickness, and that of the left, 18 mm. The epicardium was covered by a dull, granular exudate. There was a fusiform bulge in the descending ramus of the left coronary artery. This measured 7.5 mm. in diameter, and was situated 7.5 cm. distal to the left coronary ostium. There was a similar, smaller bulge in the terminal branch of the left circumflex ramus, and another in the terminal branch of the right coronary artery. The exudate over these bulges was thicker than elsewhere, and small hemorrhages could be seen in the surrounding subepicardial fat. Sections through these bulges showed that in each instance the artery was plugged with soft, friable, mottled, yellowish-gray and pale-brown debris which was loosely attached to the intima. Proximal and distal to the occlusions the vessels contained only post-mortem blood clots and showed no arteriosclerosis. Involving the apex of the left ventricle and the interventricular septum there was a well-circumscribed infarct which measured 6 cm. across. In this area the ventricular wall was thinner than elsewhere, and the muscle was mottled yellowish-brown and dusky gray. The endocardium lining all chambers was normal except in the region of the infarct, where it was thickened and opaque. The anterior mitral leaflet was severely deformed by bulky, grayish-brown vegetations which were firmly attached to its margin, and the central portion of the leaflet was ulcerated. The vegetations extended downward on the chordae tendineae to the tips of the papillary muscles, and a few of the chordae were ruptured. The posterior mitral leaflet was thickened at the right commissure, but was otherwise normal. The remaining valves showed no evidence of endocarditis.

The aorta was of normal thickness and elasticity. There were edema of the lungs, cloudy swelling of the parenchymatous organs, and acute hyperplasia of

the spleen. There were infarcts of the spleen and both kidneys. The kidneys were large, swollen, and pale pinkish-yellow. Their surfaces were dotted with tiny hemorrhages, and the striations as seen on the cut surfaces were indistinct. There were small petechiae in the mucosa of the renal pelves, the urinary bladder, and the gastrointestinal tract. A few were seen in the pia-arachnoid over the frontal and parietal lobes.

Microscopic examination of a section of the affected portion of the anterior mitral leaflet showed that the vegetations had the characteristics of those of endocarditis lenta. They were composed of undulating layers of fibrin, necrotic debris, and bacteria which stained poorly. There were small areas of ulceration, tiny thrombi attached to the surface, and a gradual transition through granulation tissue into the substance of the valve leaflet. There was nothing to establish the existence of rheumatic endocarditis. Sections through the occluded arteries showed that they were distended with plugs of fibrin, debris, and bacteria identical with those in the vegetations. The lumina were greatly enlarged. The walls were thin, as if stretched, and were the seat of severe, acute, exudative arteritis. The surrounding fat was densely infiltrated by polymorphonuclear leucocytes, and the epicardium was covered by a thick layer of acute inflammatory exudate. Proximal and distal to the occlusions the coronary arteries were normal. The changes in the myocardium were those characteristic of a septic infarct.

The kidneys were the seat of acute focal glomerulonephritis. *Streptococcus viridans* was recovered from the heart's blood and from the vegetations on the mitral valve.

The diagnosis was subacute bacterial endocarditis of the mitral valve, with discharge of emboli, occlusion of the left descending and terminal branches of the left circumflex ramus and right coronary artery, and infarction of the apex of the left ventricle.

CASE 2.—F. Z., a white man, 44 years of age, who entered Cleveland City Hospital Oct. 3, 1931, complained of fever and chills. The patient had been in excellent health until one month earlier, when he had begun to have malaise, weakness, anorexia, nausea, vomiting, severe generalized abdominal pain, lumbar backache, fever, and chills. Two days thereafter his legs started to swell and he became short of breath. After two weeks the abdominal and back pain decreased in severity, but the other symptoms became worse. There was no thoracic pain at any time.

Examination showed that the patient was well developed and well nourished, but acutely ill. The temperature was 40° C., the pulse rate was 120 per minute, and the respiratory rate was 40 per minute. There were numerous petechiae in both conjunctivae. There were râles in the bases of both lungs. The cardiac activity and sounds were feeble. A protodiastolic gallop rhythm was present, and there was a question whether or not a pericardial friction could be heard. The cardiac mechanism was normal, and the blood pressure was 100/60. The abdomen was distended, and there was fullness in the region of the liver. The legs and sacral region were edematous.

The erythrocyte count, hemoglobin value, and blood urea nitrogen level were normal. The blood Kline test for syphilis was negative. The leucocytes numbered 11,000 per cubic millimeter. The urine contained albumin (grade 3) and leucocytes (grade 1). The blood culture yielded a *Staphylococcus albus* on two occasions. The electrocardiogram in the conventional leads showed an elevation of the ST segment in Lead I and depression of the ST segment in Leads II and III.

The patient became progressively worse and died on the second hospital day. The clinical diagnosis was recent coronary thrombosis with myocardial infarction, myocardial insufficiency, septicemia due to *Staphylococcus albus*, and bronchopneumonia.

Autopsy Findings.—(Autopsy No. 7764, performed by Dr. C. J. Farinacci, four hours after death.) The body was that of a well-developed, obese, white man, approximately 45 years old. There were numerous petechiae in both conjunctivae, but none was seen in the skin. The heart weighed 475 gm. and was moderately dilated. Except for a dull, granular, dark-red patch, 3 cm. in diameter, near the apex of the left ventricle, the epicardium was smooth and transparent. The myocardium was of normal color except in the anterior, apical portion of the left ventricle, where there was a recent infarct. The affected muscle was dark-red and softer than normal. The endocardium lining all chambers was smooth. The mitral leaflets were thickened and fibrotic, particularly along their free margins. The aortic leaflets were also thickened, and nodular vegetations varying in diameter from 1.5 to 5 mm. were attached to the margin of each. The tricuspid and pulmonic valves were normal. There were a few atheromatous plaques on the intima of the coronary arteries, but their walls were not significantly thickened. The lumen of the terminal branch of the left descending ramus was occluded by an embolus lodged just proximal to the infarct.

The aorta was normal except for slight arteriosclerosis about the ostia of the intercostal arteries. There was passive hyperemia of the lungs and abdominal viscera. The spleen was the seat of acute hyperplasia, and recent infarcts were present in the spleen and both kidneys. Small hemorrhages stippled the mucosa of the renal pelves, the urinary bladder, and the gastrointestinal tract. The brain and spinal cord were normal.

Microscopically, the lesion in the myocardium had all of the features of a septic infarct; there were many clumps of cocci in pairs and packets between the necrotic muscle fibers and in the capillaries. The coronary arteries beyond the occlusion showed small patches of intimal thickening and hyalinization, but in none of the sections examined had this disease significantly reduced the caliber of the lumen. The infarcts in the spleen and kidneys also contained clumps of bacteria.

This was a case of acute endocarditis superimposed upon an old rheumatic endocarditis of the aortic valve, with an embolus plugging the terminal branch of the descending ramus of the left coronary artery and a septic infarct of the anterior, apical portion of the left ventricle.

CASE 3.—C. L., a white man twenty-six years of age, who entered Cleveland City Hospital Dec. 21, 1918, complained of "heart trouble." The patient was known to have had rheumatic heart disease since an attack of rheumatic fever at the age of 19. During the three months previous to admission he had had malaise, weakness, anorexia, night sweats, and fever, and had lost 45 pounds in weight.

Examination showed that the patient was normally developed, but poorly nourished and acutely ill. The temperature was 38° C., and the pulse rate was 114 per minute. The eyegrounds and conjunctivae were normal. The heart was enlarged both to the right and left. There were systolic and diastolic murmurs at the apex and at the aortic area. The cardiac mechanism was normal, and the blood pressure was 148/78. The lungs were normal. The edge of the liver was 3 cm. below the costal margin; the spleen was enlarged to percussion but could not be palpated.

Roentgenologic examination of the chest showed that the heart was enlarged in all dimensions. The erythrocytes numbered 2,500,000 per cubic millimeter, and the value of the hemoglobin was 50 per cent. Urinalysis was negative except for albumin (1 plus). Numerous blood cultures failed to show any growth.

The patient became progressively worse. The fever was intermittent, the temperature varying from 36° C. to 39.5° C. On March 2 he complained of sudden, severe pain in the lower part of the left leg. The dorsalis pedis artery was found to be pulseless, and in the next two weeks the left foot and toes showed ischemic necrosis.

At 8:00 A.M. on April 27 the patient suffered severe upper thoracic pain which radiated to the epigastrium and was relieved only by morphine. The following day, at 2:30 P.M., he died suddenly.

The clinical diagnosis was rheumatic heart disease with mitral stenosis and insufficiency and aortic insufficiency, cardiac hypertrophy and dilatation, bacterial endocarditis, and embolism of the left dorsalis pedis artery with ischemic necrosis of the toes of the left foot.

Autopsy Findings.—(Autopsy No. 1106, performed by Dr. Maurice L. Richardson.) The body was that of a poorly nourished white man. There was ischemic necrosis of the left foot and the great toe was mummified.

The heart weighed 630 gm. and was dilated, particularly on the right side. The epicardium was normal. The myocardium was pale and showed diffuse fibrosis, but there were no infarcts. The mitral valve was severely deformed, and the orifice measured only 2.5 cm. in diameter. Both leaflets were greatly thickened and the chordae tendineae were robust and rigid. There were bulky, gray vegetations on the free margins, with ulceration of both leaflets. The aortic leaflets were thickened, deformed, and fused at the left posterior commissure. There were vegetations and ulcers on the posterior and left anterior leaflets, and the process had extended into the aorta to a point 5 mm. above the aortic sinuses. The tricuspid and pulmonic valves were anatomically normal. At the bifurcation of the left coronary artery there was an embolus which completely occluded the descending ramus.

The thoracic and abdominal segments of the aorta were normal. The left posterior tibial artery was partially filled with a soft necrotic mass. Its wall was ulcerated and had perforated at one point to give rise to a large hematoma between the calf muscles. There was severe chronic passive hyperemia of the lungs and liver. The spleen was the seat of acute hyperplasia, and the spleen and left kidney contained septic infarcts.

Microscopic sections revealed small collections of polymorphonuclear leucocytes scattered throughout the myocardium. These were usually situated in the supporting connective tissue, frequently near small blood vessels. The muscle fibers were large, and many of the nuclei had square poles. There was considerable fragmentation, but the striations were preserved. The infarcts of the spleen and left kidney were typical, and random sections of the kidneys showed acute focal glomerulonephritis.

The diagnosis was chronic rheumatic heart disease, superimposed subacute endocarditis of mitral and aortic valves with extension of the vegetations upward about the ostia of the coronary arteries, and embolism of the left coronary artery with occlusion of the descending ramus.

COMMENT

Clinically, the first case was typical of subacute bacterial endocarditis except that numerous blood cultures were negative. There was nothing during life to suggest myocardial infarction or coronary embolism. The absence of pain would suggest that the infarction was painless or that the patient's sensibility was so blunted that he did not appreciate pain. The electrocardiogram was normal but had been taken one month before death. Post-mortem examination, however, established the fact that coronary embolism was present. There were ulcerated vegetations on the mitral valve, and the embolus was histologically indistinguishable from these vegetations. The wall of the

coronary artery showed only such changes as were secondary to the embolus, and the resulting infarct was septic. The case was unusual in that death was not sudden, and infarction had occurred. The presence of three distinct emboli was also noteworthy.

In the second case, clinically, there was evidence of infarction and septicemia; the two processes, however, were not thought to be related. Post-mortem examination established the diagnosis in this case, also; the vegetative endocarditis of the aortic valve was an obvious source for the embolus, the wall of the occluded vessel was normal, and there was a septic infarct in the myocardium.

In the third case, the sudden death of a patient known to have rheumatic heart disease, bacterial endocarditis, and embolic occlusion of an artery of an extremity might well have been thought to be due to coronary embolism, but sudden death in cases of heart disease can result from other causes, so that even in retrospect a clinical diagnosis of embolism would not seem justified. The ulcerative endocarditis of either the mitral or aortic valves was the source of the embolus, and no other cause for occlusion of the coronary artery was demonstrable.

SUMMARY

Three cases of coronary embolism were encountered among 12,300 consecutive autopsies at Cleveland City Hospital. In none was the diagnosis made clinically. The source of the emboli in each instance was an ulcerative endocarditis of either the aortic or mitral valves. Myocardial infarction occurred in two cases.

ADDENDUM

Since this paper was submitted for publication, one of the authors (J. L. W.) has examined another case of coronary embolism at the St. Alexis Hospital of Cleveland, Ohio. The patient, a white man, 45 years of age, who was considered to have subacute bacterial endocarditis because a blood culture had yielded a growth of *Streptococcus viridans*, died suddenly while being moved in a wheel chair. The autopsy revealed hypertrophy and dilatation of the heart and subacute bacterial endocarditis of the aortic valve. Two emboli, composed of material identical with that on the heart valves, were present in branches of the descending and circumflex rami of the left coronary artery. The branch of the descending ramus was occluded at its origin, and the circumflex ramus at its bend into the posterior longitudinal sulcus. Proximal and distal to the occlusions both arteries were normal. There was no infarction of the myocardium.

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Department of Clinical Reports

BACTERIAL ENDOCARDITIS DUE TO THE STREPTOCOCCUS FECALIS

Report of a Case

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THE *Streptococcus viridans* is commonly mentioned as the causative organism in cases of subacute bacterial endocarditis (recurrent endocarditis, endocarditis lenta), with occasional reference to the gonococcus, influenza bacillus, and others, as organisms capable of producing the disease in rare instances. Careful search of the Index Medicus and Catalogue of the Army Medical Library revealed several reports of cases of enterococcal endocarditis, but none in which the *Streptococcus fecalis* was named as the causative agent. Since the enterococci comprise a large group, of which *Streptococcus fecalis* is a member,[1] it is possible that several of the reported cases were caused by the latter organism. With one exception,[2] the reports appeared in foreign journals. The purpose of this paper is to present a case on the borderline between acute and subacute bacterial endocarditis, in which careful bacteriologic studies identified the causative organism as *Streptococcus fecalis*.

Streptococcus fecalis was first described by Andrewes and Horder, in 1906,[3] and its classification worked out on the basis of earlier investigations by Gordon (1903-4). Andrewes and Horder found the organism in the blood before and after death in four out of twenty-four cases of "malignant" endocarditis. They considered it an organism of rather feeble pathogenicity, closely related to *Streptococcus salivarius* (a species of the viridans group), one passing into the other "by insensible gradations." This conception of a very close relationship has been held by many later writers. It is hardly necessary to mention the difficulties involved in classifying the streptococci, nor will space permit a discussion of this problem. However, recent work by Sherman[4] makes possible a more decisive separation of *Streptococcus fecalis* from members of the viridans group.

Streptococcus fecalis belongs to the large group of streptococci known as the enterococci, which are characterized by heat resistance, bile tolerance, and the ability to ferment manitol. Sherman[5] points out the inadvisability of classifying streptococci by their action on blood alone. He considers as hemolytic only those organisms which produce a clear-

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The bacteriologic studies were carried out by Drs. W. D. Eaton and W. G. Stewart.
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cut beta hemolysis; all others, which produce the lesser degrees of hemolysis designated as alpha and gamma, are considered nonhemolytic. Thus both *Streptococcus viridans* (alpha hemolysis) and *Streptococcus fecalis* (gamma hemolysis) fall into the "nonhemolytic" group, and Sherman has stated that "the question of how frequently strains of *Streptococcus viridans* isolated from cases of endocarditis are in fact organisms of another group is as yet unanswered." Recently, further evidence, based on serologic reactions, justifying the division of the enterococci from the viridans group has been offered by Sherman,[4] who sought to extend the unpublished observations of Lancefield (1937). She had found that cultures of *Streptococcus fecalis* and *Streptococcus liquefaciens*, both members of the enterococcus group, belonged serologically to the Lancefield Group D. Sherman worked with more than fifty cultures of *Streptococcus fecalis*, identified by physiologic studies. The strains were taken from human feces, milk, ice cream, and cheese, and they included organisms from the blood in this case, sent by Dr. E. G. D. Murray. In each instance, the strains were found to belong to Lancefield Group D. Furthermore, similar work done on *Str. liquefaciens* and *Str. durens*, both recognized members of the enterococcus group, placed those organisms in Lancefield Group D. *Str. zymogenes*, a fourth recognized species of enterococcus, was first used to establish Lancefield Group D. Members of the viridans group (*Str. salivarius*, *Str. equinus*, etc.) are serologically heterogeneous.

REPORT OF CASE

History.—Mrs. B. L., a French Canadian, aged 30, was admitted to the service of Dr. C. F. Moffat, Royal Victoria Hospital, Nov. 15, 1937. She had had attacks of fever with polyarthritis, diagnosed as rheumatic fever, which began at the age of three and recurred every winter for ten years. At the age of seven, she had severe choreiform movements and extreme nervousness, necessitating her admission to a hospital. At the age of 25 she had another attack of polyarthritis and fever. Three years later, at the age of 28, she became pregnant and began to show signs of cardiac decompensation. She was dyspneic and orthopneic and was forced to spend a long period in bed following delivery. She then enjoyed fairly good health until August, 1937, two years later, at which time she had a spontaneous abortion in the second month of pregnancy. In the same month, two feet of segmented flatworm were passed after the administration of an anthelmintic. In the middle of September, 1937, she had an attack of acute polyarthritis involving the left extremities, associated with weakness, anorexia, and nausea with occasional vomiting. After two weeks of rest in bed the polyarthritis disappeared, but during the succeeding two weeks the number of her bowel movements increased to three or four a day, defecation was accompanied by tenesmus, and the stools were watery and green. At the same time she began to notice rather severe pain in both upper quadrants of the abdomen. This state of affairs continued until the day of her admission to the hospital, Nov. 15, 1937, two months after the onset of the attack of acute polyarthritis. She observed a tender, slightly reddened elevation on the medial surface of her right thumb one week prior to admission, and a change in the appearance of her urine, which became the color of porter four days before admission. There had been a weight loss of 15 pounds in the two preceding months.

Two brothers and one sister had had rheumatic fever. The past history and functional inquiry revealed nothing of additional significance.

Physical Examination.—The temperature was 98°F., the pulse rate 120, and the respiratory rate 45. The patient was an emaciated and pale young woman, markedly dyspneic. The skin had the so-called café-au-lait appearance, but this was said to be her usual color. There was slight clubbing of the fingers, but no peripheral edema. The teeth were carious, and there was a marked gingivitis. Examination of the cardiovascular system revealed a rapid, regular pulse of poor volume; pulsation of the neck veins; an apical diastolic thrill; enlargement of the heart to percussion; a loud, booming first sound with a mitral presystolic murmur at the apex; a soft, blowing diastolic murmur at the pulmonic area; and softening of the aortic second sound, with a suggestion of a diastolic murmur. The blood pressure was 108/52. The chest expanded normally on both sides. There were fine crepitations at the left base posteriorly, but the lungs were otherwise normal to percussion and auscultation. There was generalized tenderness over the abdomen, and the liver and spleen were palpable below the costal margin, the former for a distance of four, the latter for a distance of three, fingerbreadths. Examination of the locomotor and nervous systems contributed nothing of (diagnostic) significance. No petechiae were seen at any time. The clinical impression formed from the above findings was that she had rheumatic heart disease of long standing, with a moderate degree of decompensation, mitral stenosis and insufficiency, aortic insufficiency, and subacute bacterial endocarditis.

Laboratory and Special Examinations.—The urine was acid in reaction, had a specific gravity of 1.020, and contained albumin (4 plus), acetone (2 plus), 6 to 10 leucocytes per high-power field, and great numbers of erythrocytes. The hemoglobin was 58 per cent (9 gm.), the erythrocyte count 3,400,000 and the leucocyte count 12,600. The uric acid content of the blood was 4.84 mg. per cent, the nonprotein nitrogen, 44 mg. per cent, the total protein nitrogen, 940 mg. per cent, and the sugar, 159 mg. per cent. The electrocardiogram showed normal rhythm, normal A-V conduction time, low voltage of the QRS complexes, and depression of the S-T intervals in Leads I and II. A blood culture taken on the day of admission yielded a pure culture of organisms which were at first placed tentatively in the enterococcus group because of their heat resistance. Further physiologic studies identified the organism as *Streptococcus fecalis.* A strain was sent to Dr. J. M. Sherman, who confirmed the classification and carried out the studies mentioned above, in which this organism, along with others of the same species, was found to belong to Lancefield Group D. Another blood culture, taken a few days later, gave identical results.

Progress.—The patient grew steadily worse, and died November 25, ten days after admission and approximately ten weeks after the onset of the final episode. The temperature fluctuated between 101 and 104° F., with progressive pallor, weakness, and prostration, and increasing splenomegaly, abdominal tenderness, and distention.

Autopsy.—The heart was not enlarged (300 gm.). Focal fibrous pericardial adhesions were seen between the pulmonary artery and right auricular appendage. The left ventricular myocardium was dark red, soft, and its wall measured only 1 cm. in thickness. The mitral valve showed diffuse thickening of the cusps and slight narrowing of the orifice (8 cm.), with projecting, friable, pale gray polypoid vegetations along the free edge, almost filling the valve opening. The anterior and left posterior cusps of the aortic valve were thickened and fused, presenting at the point of fusion many smaller, but similar, vegetations.

Microscopic Examination.—Sections from the left ventricular wall showed a focal productive myocarditis, with occasional nodules of large, pale cells lying in perivascular tissue. No Aschoff bodies were seen. Sections from the left auricle

showed marked fibrous thickening of the endocardium and some hypertrophy of the muscle. Examination of the polypoid vegetations and the underlying valvular tissue revealed marked, hyaline, fibrous-tissue thickening of the valve, surmounted by a large mass composed of laminated fibrin containing many disintegrating leucocytes, and a zone of granulation tissue. There was a marginal mass of fibrin containing many cocci arranged in short chains and pairs, staining a deep blue with Gram's stain. There were several other interesting autopsy observations. The spleen was only slightly enlarged (155 gm.), and showed an extremely soft, necrotic middle third, with the capsule everywhere intact. The microscopic appearance was typical of infarction.

The peritoneal cavity contained 100 c.c. of thick, purulent material, and the parietal peritoneum over the left lateral and posterior surfaces showed a diffuse reddening which involved loops of bowel, as well. The spleen was attached to the diaphragm above, and to the transverse colon below, by fragile, fibrinous adhesions. These findings pointed to a direct relationship between the large splenic infarct and the peritonitis.

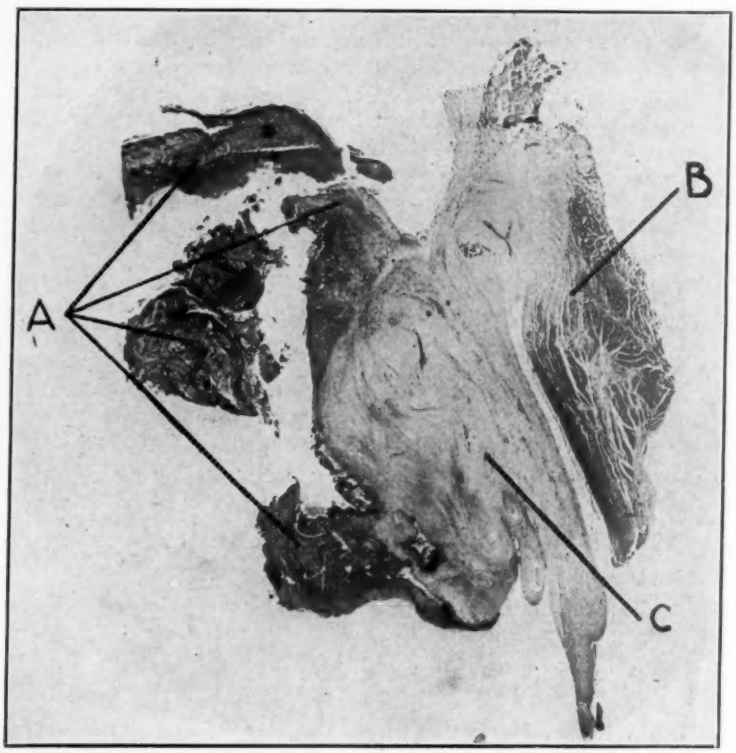

Fig. 1.—Low-power view of mitral valve with recent vegetation. *A*, recent vegetation (fragmented); *B*, wall of left ventricle; *C*, greatly thickened mitral valve (old productive endocarditis).

Each pleural cavity contained approximately 250 c.c. of slightly bloodtinged, turbid fluid. Both lungs showed a patchy pneumonia.

The small bowel showed scattered areas of injection, and contained a long, yellow tapeworm, identified as *Taenia saginata*. The head of the worm was not attached to the mucosa of the bowel at the time of autopsy.

One of the mesenteric arteries showed panarteritis with thrombosis, but there was no evidence of infarction in the area of small bowel supplied by that artery.

A typical, focal, exudative nephritis was present, together with a small, anemic infarct in the right kidney.

The liver was the seat of passive congestion.

The brain showed scattered capillary thrombi and small perivascular hemorrhages.

Bacterial cultures taken from the valvular vegetations at autopsy yielded a pure growth of *Streptococcus fecalis.*

Anatomic Diagnosis.—Productive and fibrinous polypoid endocarditis, mitral and aortic valves; mitral stenosis; focal productive myocarditis; productive pericarditis, localized; patchy pneumonia, bilateral; massive septic infarct, spleen; fibrinous and purulent peritonitis; tapeworm, small intestine *(Taenia saginata);* focal exudative nephritis; septic infarct, right kidney; passive congestion, liver; panarteritis, mesenteric artery, with septic thrombosis.

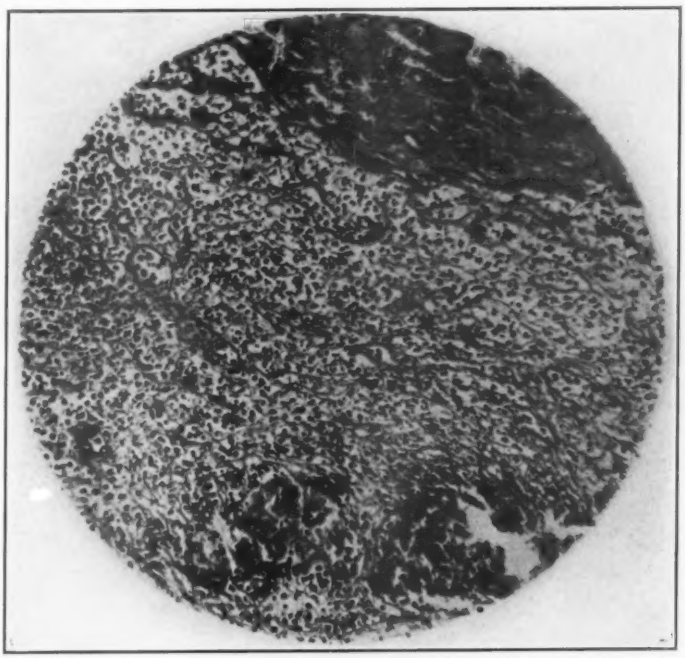

Fig. 2.—High-power view of mitral vegetation. Disintegrating leucocytes are held in a fibrin meshwork.

DISCUSSION

This case stands on the borderline between acute and subacute bacterial endocarditis. There was a history of previous rheumatic valvular disease, followed by an attack which had rather vague beginnings and ended in death, after running a course of approximately nine to ten weeks. The final illness was characterized, chiefly, by weakness, lassitude, dyspnea, anemia, vague pains, fever, loss of weight, clubbing of the fingers, and by outward evidences of embolic phenomena, enlargement of the spleen, and hematuria with albuminuria. Petechiae were not observed while the patient was in the hospital. However, she noticed a

tender, red elevation on her right thumb one week before admission. This may have been an Osler's node. The autopsy findings confirmed the clinical diagnosis.

Another feature worthy of note was the peritonitis, which was confined mostly to the left side and apparently related to a massive splenic infarction. Several instances of peritonitis following rupture of the spleen in cases of subacute bacterial endocarditis have been reported, but in this case the capsule of the organ was found intact at autopsy. It is reasonable to suppose that the infecting organisms passed from the necrotic infarcted area through the capsule to the abdominal cavity. Clinical examination revealed that abdominal tenderness and rigidity of the abdominal muscles were observed several days before death.

Of interest also, was the discovery of a long tapeworm in the small intestine. This may explain the diarrhea, which was of fairly long standing.

The isolation of *Streptococcus fecalis* from the blood stream in life, and from the mitral vegetations at autopsy, is the most noteworthy feature. It raises a question, discussed briefly above: How frequently is subacute bacterial endocarditis caused by *Str. fecalis* or other organisms of the enterococcus group? Judging from the literature, the occurrence is rare. There is some reason to believe that it may be more frequent than is generally suspected, as careful bacteriologic work is necessary for the proper identification of the organism.

SUMMARY

1. A case of *Streptococcus fecalis* endocarditis, with autopsy findings, in a 30-year-old woman with rheumatic valvular disease, is reported.

The organism was isolated from the blood stream during life, and from the heart valves at autopsy.

2. Peritonitis caused by splenic infarction without rupture of the spleen was observed.

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THE CARDIAC MECHANISM IN A FATAL CASE OF ACUTE THYROTOXICOSIS

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THE role of the thyroid gland in the production of cardiac dysfunction, and even cardiac failure, is well recognized. That the cardiac derangement may be the only apparent clinical manifestation of hyperthyroidism was brought out by the investigations of Levine and Sturgis, in 1924.[1] Recently we have been afforded the opportunity of observing the terminal cardiac mechanism during a thyroid crisis which ended fatally. The electrocardiographic studies were made during the last few hours of life, and we believe that they record the mode of cardiac death in thyroid crisis more accurately than tracings[2] which have shown only the last few heart beats after the patient was, from the clinical point of view, dead.

CASE REPORT

B. W. S., Med. No. 54135, a 41-year-old, unemployed white man, entered the hospital for the first time Dec. 27, 1938, complaining of generalized weakness. He had been well until October, 1938, at which time he noted the onset of a nonproductive cough, mild fever, and generalized prostration, severe enough to confine him to bed intermittently. Fluoroscopic and roentgenographic examinations of the chest were reported as negative by his family physician. He became increasingly irritable, apprehensive, and fatigued. In December, 1938, he had a low-grade, intermittent fever, associated with a systolic murmur at the apex, but without other cardiorespiratory symptoms. He had been sleeping well, had had only a fair appetite, and had lost approximately twenty pounds in the preceding two years. The past history was unimportant. The family history was significant only in that his father had died of angina pectoris and his mother had active pulmonary tuberculosis. The marital and social history revealed much domestic conflict. He had been unemployed for two years, during which time he had been dependent upon friends and relatives.

Physical Examination.—The patient was a restless, well-developed, well-nourished, middle-aged man. He was agitated, but his speech was coherent and his mentality clear. His temperature was 99.2° F., his pulse rate 96, and his respiratory rate 25. The skin was warm and moist. The palms, axillae, and groins were bathed in sweat. Examination of the eyes, including the fundi, was negative. There was no exophthalmos or lid-lag. The thyroid gland was not enlarged to palpation, and presented no bruit. The lungs were negative. The heart was not enlarged; the apex impulse was forceful and diffuse. The retromanubrial dullness was not increased. The cardiac rhythm was normal. The first sound was snapping in character, with a moderately loud systolic murmur, most intense at the apex. There were no diastolic murmurs. The blood pressure was 170/100. The deep reflexes were hyperactive, but equal. The extended fingers showed a fine tremor. The remainder of the examination was negative.

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Laboratory Examination.—The urine, blood, and stool were normal. The blood Wassermann reaction was negative. The corrected sedimentation rate was within normal limits. *Streptococcus hemolyticus* skin tests showed the presence of sensitivity. Two blood cultures remained sterile. The basal metabolic rate (Dec. 29, 1938) was plus 32. Roentgenologic examination of the chest was negative, showing no evidence of substernal thyroid enlargement.

Clinical Course.—The patient's course in the hospital was uneventful. The pulse rate ranged between 90 and 100 during his four-day stay. He was thought to have mild hyperthyroidism and was advised to remain for further observation to confirm the diagnosis. However, on his wife's insistence, he left the hospital against advice, with permission to return.

(Second Admission, Med. No. 54430). The patient re-entered the hospital Feb. 11, 1939. During the interim, after feeling well for one week after discharge, he had suffered a recurrence of all his previous symptoms. Nervousness was now associated with sleeplessness and mild palpitation. He had maintained his weight, although his appetite remained only fair. Two days prior to entry he was in an automobile accident in which he suffered no obvious physical trauma. However, he claimed to have undergone a severe emotional shock, necessitating his confinement to bed. Subsequent information revealed that a damage suit had been instituted.

Physical Examination.—The patient was much more agitated and voluble than on his first admission. One observer felt that there was slight exophthalmos. The thyroid now showed slight diffuse enlargement but presented no bruit. The heart was essentially the same as at the first examination. The blood pressure was 122/68. The heart rate was 125, the rhythm normal. The tremor of the fingers was more noticeable. The remainder of the examination revealed nothing not present on the first admission.

Laboratory Examination.—The basal metabolic rate was plus 65 and plus 70, on Feb. 13 and Feb. 14, respectively. Other studies showed nothing abnormal.

Clinical Course.—The patient's condition remained essentially unchanged until the evening of Feb. 14, at which time he became very agitated, jumping in and out of bed, attempting to leave the hospital, weeping loudly, and apparently suffering from an acute hallucinosis. He became unmanageable, and required sedatives and restraints. On Feb. 15, the administration of Lugol's solution, in doses of 10 minims three times daily, was begun. He continued to be hyperactive despite the administration of sedatives, and fluids parenterally. Some observers felt that he was suffering from a toxic delirium, possibly secondary to his repeated medications rather than to his hyperthyroidism. Accordingly, all medications except iodine were withdrawn for a twelve-hour period, and fluids were forced parenterally. He continued to grow worse on this regimen. It became necessary to use paraldehyde in frequently repeated doses. On Feb. 17 and 18, Lugol's solution was given intravenously in 3.0 c.c. doses, in addition to that given orally. When not under the influence of sedatives, the psychotic manifestations reappeared. During this period of time the temperature ranged between 98.2° and 100.4° F., the pulse rate between 90 and 125, the respiratory rate between 30 and 45, and the blood pressure remained near the admission level.

On Feb. 18, at 10:40 P.M., the radial pulse suddenly became thready, and the patient appeared dusky and cyanotic. The respirations were rapid and shallow, remaining so in spite of the administration of oxygen intranasally. Auscultation of the heart revealed a regular apical rate of 180, uninfluenced by vagal stimulation. At 10:50 P.M., the heartbeat had become absolutely irregular, with a ventricular rate between 250 and 325 (Fig. 1*a*). At 11:00 P.M., the cardiac mechanism abruptly changed spontaneously to a slow normal sinus rhythm, with a rate of 79.6 (Fig. 1*b*). Thereafter the rate increased gradually until a dominant rate of 195 became established (Fig. 1*c* and *d*). The blood pressure at this time was 110/70. At

11:30 P.M., 10 c.c. (0.5 gm.) of "digalen" were administered intravenously. Auscultation and serial electrocardiograms revealed no changes in the cardiac mechanism. A second 10 c.c. (0.5 gm.) dose of "digalen" was injected intramuscularly at 12:45 A.M. An electrocardiogram fifteen minutes later revealed persistence of the normal sinus tachycardia, with a rate of 145.2 (Fig. 1*e*). At 1:04 A.M., he suddenly became very cyanotic, the heart sounds became very weak and distant, and the blood pressure unobtainable. At this time the apical rate was 100. Within two minutes, coarse bubbling râles appeared throughout both lungs, the heart tones were not heard, and respirations ceased. Artificial respiration and stimulants were of no avail. Electrocardiograms taken during this final interval (Fig. 1 *f* and *g*) revealed marked sinus bradycardia and ventricular standstill.

Summary of Post-mortem Examination.—The *heart* weighed 350 gm. There was no evidence of enlargement, hypertrophy, or dilatation. The valves were thin, membranous, freely movable and showed no vegetations. The posterior cusps of the aortic valves were fused for a distance of 0.8 centimeter; the valve margins were not rolled. The myocardium was a deep reddish brown, with no evidence of fibrosis or infarction. The coronary arteries were patent. *Lungs:* The right lung weighed 550 gm., the left, 620 gm. The cut surfaces of the lungs showed uniform, marked, passive congestion, without evidence of pneumonia. The *liver* weighed 1540 gm. Its consistency was soft, and it had a light reddish-brown color and a faintly granular surface. The capsule was thin, shiny, and glistening. The cut surface showed a sharp edge, with well-differentiated liver markings due to congestion and closely resembling the nutmeg mottling of cardiac cirrhosis. There was no evidence of bile stasis, foci of necrosis, or thrombosis. The thyroid gland weighed 57 gm. It was symmetrically enlarged, with evidence of hyperplasia and increase in colloid. There was a small cystic area at the right upper pole, but no evidence of fibrosis or inflammation.

Microscopic Examination.—The myocardium showed no inflammatory reaction or increase in connective tissue stroma. There was considerable edema of the interstitial tissues. No Aschoff bodies were seen. No areas of true degeneration of muscle fibers were found. Lungs: The veins were moderately engorged. The alveolar walls were slightly swollen. Liver: There was an apparent increase in connective tissue in many of the central areas. There were recent infarcts of varying size, about central or mid-zone in location; the cord cells in these areas were pale red, the erythrocytes having faded. No thrombi were seen. There was no increase in periportal connective tissue. Thyroid: The acini varied in size and shape: most of them contained large masses of desquamated epithelial cells, mixed with colloid varying from pale pink to deep blue. Better preserved acini showed infolding of epithelium, and its tall columnar type was evident. The stroma was not increased.

Anatomic Diagnosis.—Hyperplasia of thyroid, with slight iodine involution; edema of lungs; focal infarcts of liver; passive congestion of lungs, liver, spleen, and kidneys; cirrhosis of liver (cardiac); hyperplasia of thymus; hyperplasia of aberrant thymus; congenitally bicuspid aortic valve.

DISCUSSION

The frequency of paroxysmal auricular fibrillation in hyperthyroidism has been commented upon by many investigators, among them Barker, et al.,[3] Nicholson,[4] Ernstene and Mulvey,[5] and Hay.[6] In our case the cardiac mechanism remained normal, although the rate was rapid, until the terminal episode, during which paroxysmal auricular fibrillation with an extremely rapid ventricular rate appeared. It was observed that,

just prior to the first electrocardiogram here reproduced, the heart rate changed abruptly from 125 to 180. The beating was regular, there was no pulse deficit, and vagal stimulation was without effect. Within ten minutes the beating became completely irregular. The electrocardiogram taken at that time (Fig. 1*a*) shows auricular fibrillation with a ventricular rate ranging between 250 and 300; in places, small groups of beats reached a rate of 325. At one point in Lead I (marked *X*), there are two consecutive beats which we interpret as ventricular extrasystoles. They resemble beats which inaugurate ventricular tachycardia. Following the maintenance of fibrillation at this rapid rate for ten minutes, there was an abrupt, spontaneous change to a slow, normal, sinus rhythm (Fig. 1*b*), which became progressively more rapid until it

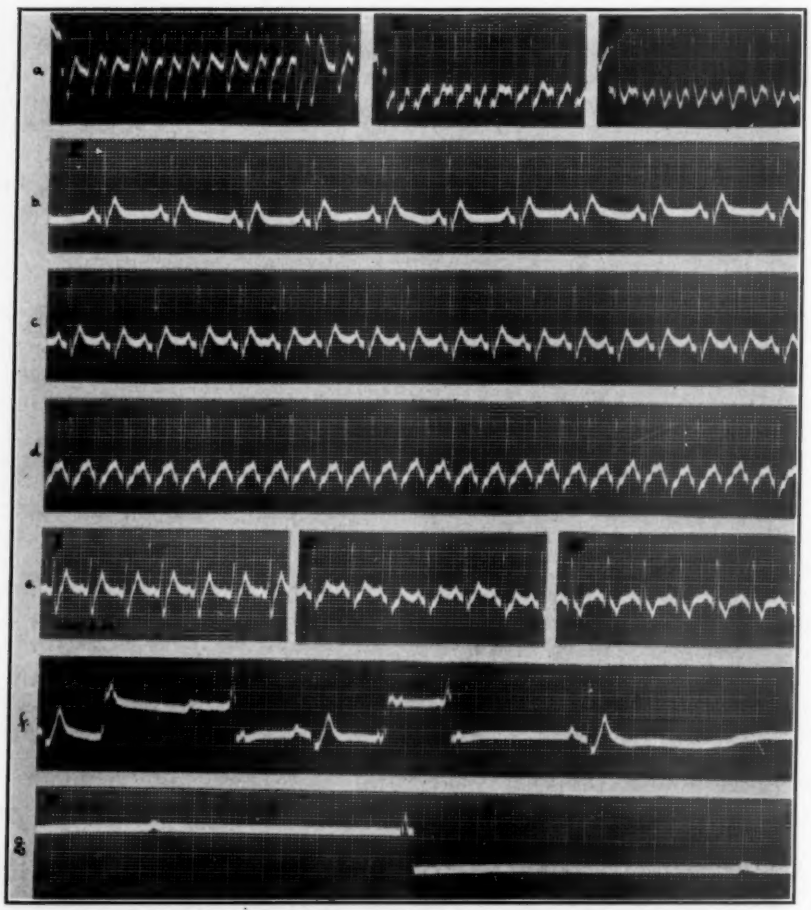

Fig. 1.—Electrocardiographic records during final hours of life in a case of acute thyrotoxicosis. *a*, 10:50 P.M., auricular fibrillation, ventricular rate 250 to 325. Ventricular extrasystoles marked *X* in Lead I. *b*, 11:01 P.M., normal sinus rhythm, ventricular rate 79.5, with peculiar, short duration of R-T complex. *c*, 11:02 P.M., sinus tachycardia, ventricular rate 125.8. *d*, 11:25 P.M., sinus tachycardia, ventricular rate 196.6. *e*, 1:00 A.M., patient had received 20 c.c. (1.0 gm.) of "digalen," sinus tachycardia, ventricular rate 145.2. *f*, 1:05 A.M., the dying heart. *g*, 1:06 A.M., two minutes after death had occurred, as ascertained clinically.

reached a rate of 195.6 (Fig. 1*c* and *d*). This sinus tachycardia was only slightly affected by digitalis (Fig. 1*e*), which is the type of response to the drug observed by Barker, et al.,[3] Nicholson,[4] and Grant[7] in cases of hyperthyroidism. After the rate had been maintained for ninety-five minutes, the heart gradually slowed, and the terminal cardiac mechanism can be seen to be one of bradycardia and ventricular standstill (Fig. 1 *f* and *g*). It is of interest to note that in all of the records in which there is a normal response to the auricular impulse, the duration of the R-T complex is quite short, even when the heart rate is very slow.

A review of the literature discloses only a few reports concerning the exact character of the terminal cardiac mechanism in hyperthyroidism. Goodall[8] was of the opinion that ventricular fibrillation was the actual cause of sudden death during acute thyrotoxicosis following operation upon the thyroid gland. Cookson[9] concluded that sudden death in cases of auricular fibrillation associated with various types of heart disease was due to fibrillation of the ventricles. Willius, et al.,[10] McEachern and Rake,[11] and Hamilton[12] have reported series of patients observed clinically, and have described the mode of death in thyroid crisis. Their reports agree, in that the majority of the patients showed no clinical evidence of congestive failure, a fact borne out in the case here presented. Their case reports are uniform, in that all of the patients had rapid heart rates, though there was no consistency about the nature of the cardiac mechanism. However, in none of these published reports are we able to find electrocardiographic observations of the actual, final, cardiac mechanism. Levine[13] has pointed out that, viewing the arrhythmias of hyperthyroidism as a whole, the great majority are auricular in origin. The terminal cardiac mechanism in this case can be seen to be a rapid auricular arrhythmia, followed by bradycardia and ventricular standstill. It is suggested that death was due to exhaustion of the myocardium.

The authors wish to acknowledge their appreciation of the valuable suggestions and assistance of Dr. Samuel A. Levine in this study, and of the aid of Dr. G. Darrell Ayer in the review of the pathologic material.

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11. McEachern, D., and Rake, G.: A Study of the Morbid Anatomy of Hearts from Patients Dying with Hyperthyroidism, Bull. Johns Hopkins Hosp. **48**: 273, 1931.
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Department of Reviews and Abstracts

Selected Abstracts

Plotz, Milton: Asthmatoid Heart Failure; a Form of Left Ventricular Failure and Its Differentiation From Bronchial Asthma by Circulation Time and Other Criteria. Ann. Int. Med. **13**: 151, 1939.

Wheezing respiration is common in left ventricular failure. It may occur without basal râles (''asthmatoid heart failure'') in which case it closely simulates allergic asthma in symptoms, physical signs, and response to adrenalin.

The pathogenesis is discussed and illustrative cases are given.

The quickest and easiest method of determining whether or not a case of paroxysmal dyspnea is cardiac in origin is by means of a study of the circulation times which show decreased blood velocity in the pulmonary circuit. Arm-to-carotid (cyanide) and arm-to-lung (ether) times may be quickly and accurately determined at the bedside. They are more reliable in the differential diagnosis than determinations of the venous pressure.

AUTHOR.

Dry, Thomas J., and Willius, Fredrick A.: Interpretation of the Electrocardiographic Findings in Calcareous Stenosis of the Aortic Valve. Ann. Int. Med. **13**: 143, 1939.

The electrocardiographic findings in 176 cases of calcareous stenosis of the aortic valve are presented. The records were analyzed with special reference to graphic configurations conforming to the generally accepted laws of predominant ventricular strain. A very high correlation between electrocardiographic variations and pathologic lesions was disclosed for the post-mortem material, only eight cases proving to be exceptions to the rule.

In clinical cases the same opportunity for comparable correlations was obviously not afforded, although a similar tendency toward correlation was disclosed when the data on the post-mortem cases were applied to them.

Auricular fibrillation occurred infrequently, only twenty-five instances (14.2 per cent) being recorded for the entire series. In six cases auricular fibrillation occurred in the presence of mitral stenosis and aortic insufficiency, and in seven other cases in the presence of aortic insufficiency alone.

AUTHORS.

Helwig, Ferdinand C., and Wilhelmy, Ellis W.: Sudden and Unexpected Death From Acute Interstitial Myocarditis: A Report of Three Cases. Ann. Int. Med. **13**: 107, 1939.

Three cases of acute interstitial myocarditis causing sudden and unexpected death are reported. In all instances a laborious microscopic examination of the myocardium was necessary before the lesion was found. The necessity for painstaking histologic investigation of the myocardium in sudden death is obvious.

Acute interstitial myocarditis may be the sole cause of sudden and unexpected death.

AUTHORS.

Lowell, T. C.: The Significance of Myocardial Scars in the Human Heart. J. Path. & Bact. **49**: 195, 1939.

In a series of five cases, myocardial scars in the ventricle were reconstructed and are described in detail. These scars were shown to have an anatomic position consistent with their being a portion of one of the various muscle groupings of the ventricles. It is suggested that they represent the end stage of a type of myocardial infarction due to interference with the blood supply to a portion of a muscle bundle though not necessarily the result of coronary thrombosis of embolism.

AUTHOR.

de Navasquez, S.: The Incidence and Pathogenesis of Myocardial Lesions in Subacute Bacterial Endocarditis. J. Path. & Bact. **49**: 33, 1939.

Myocardial lesions whose characteristics have been defined, were encountered in nineteen out of twenty cases of subacute bacterial endocarditis.

These lesions develop as a result of embolism of the coronary arteries of arterioles by fragments of vegetation which vary in size and bacterial content. They are specific only insofar as they show evidence of embolism and polymorphonuclear reaction.

No relationship was demonstrated to the degree of cardiac failure, the heart valve affected, the character of the vegetation, or the duration of the disease.

AUTHOR.

Fernando, P. B.: Rheumatic Heart Disease as Met With in Hospital Practice in Ceylon. Quart. J. Med. **8**: 261, 1939.

The autopsy records of the General Hospital in Colombo, for the period of July, 1934, to November, 1937, have been studied for evidence of rheumatic carditis. The records of 215 patients admitted for rheumatic infections into the wards under the care of the author during this same period have been studied from the clinical point of view.

The post-mortem incidence of rheumatic carditis appears to be the same in Colombo General Hospital as in Guys and St. Mary's Hospitals in London. The incidence, manifestations, virulence, and progressiveness of the disease seem to be very little different from what they are in temperate climates.

The incidence of rheumatic infections was 2.2 per cent of the total admissions. The incidence of rheumatic carditis was 1.4 per cent of the total admissions and 21.5 per cent of cardiovascular admissions. Approximately one-third of the rheumatic cases had no evidence of carditis, while two-thirds had evidence of carditis. The above figures agree closely with similar figures for the five general hospitals in Victoria, Australia.

The clinical manifestations of rheumatic arthritis were in no way different from those of the conditions diagnosed as such in temperate climates.

The tendency to the occurrence of carditis was similar. Adolescents and young adults were those most liable; the manifestations of the carditis were also similar. Valvular lesions predominated as in other countries.

The commonest valvular lesion was mitral stenosis, and next in order of frequency came aortic regurgitation. Mitral lesions were eight times as numerous as aortic lesions.

Clinically evident pericarditis occurred in 6.9 per cent of the cases of rheumatic carditis.

Auricular fibrillation occurred in nearly a quarter of the patients above the age of 30 years who showed evidence of carditis. About two-thirds of the cases of auricular fibrillation were in patients with mitral stenosis. Auricular fibrillation and flutter therefore occurred in 16 per cent of all the cases of rheumatic carditis.

Uncomplicated rheumatic arthritis was commoner in males than in females, but carditis both in the acute and chronic forms occurred more frequently in the female.

Over four-fifths, both of the cases and of the deaths, were in patients below 41 years of age. The heaviest incidence was in the two age groups between 21 and 40 years. The above figures show that in Ceylon also rheumatic carditis is a disease of adolescence and early adult life, and the majority of patients so affected die before they reach the age of 40 years.

There was no greater susceptibility to rheumatic infection in any one of the races inhabiting the island.

All the cases studied were in the poorer classes of the population, and factors common to all were overcrowding and malnutrition.

The incidence of chorea in this series was only one-third of that in Victoria, Australia.

Subcutaneous rheumatic nodules were not met with; they are supposed to be rare in Ceylon.

AUTHOR.

Wood, J. Edwin, Jr., and Cash, James R.: Obesity and Hypertension: Clinical and Experimental Observations. Ann. Int. Med. 13: 81, 1939.

The literature indicates a definite association between obesity and systolic blood pressure elevation in a fair number of instances.

Systolic blood pressure in normal and hypertensive dogs rises with weight gain and falls with weight loss, while diastolic pressure varies little.

These observations do not indicate that obesity is a cause of essential hypertension but support the idea that overweight may be a factor of importance in the elevation of systolic blood pressure.

AUTHORS.

Williams, Denis, and Lennox, William G.: The Cerebral Blood-Flow in Arterial Hypertension, Arteriosclerosis, and High Intracranial Pressure. Quart. J. Med. 8: 185, 1939.

Simultaneous samples of blood were obtained from an artery and from an internal jugular vein in forty patients with high intracranial pressure, arterial hypertension, or cerebral arteriosclerosis, and from a control group of forty-one persons without any of these disorders. The blood-gas contents were determined, and the arteriovenous differences and coefficients of oxygen utilization were used to estimate the relative cerebral blood flow of the groups.

The total cerebral blood flow of the groups with arterial hypertension and high intracranial pressure was normal.

The group with cerebral arteriosclerosis had a mean cerebral blood flow of 15 per cent below that of the control group. All the individuals in this group fell within normal limits, but none had a faster flow than the normal mean, due to mechanical limitation of the vascular bed.

It is therefore concluded that the cerebral blood flow is not significantly altered by high intracranial pressure, arterial hypertension, or by cerebral arteriosclerosis without hypertension.

The mechanism whereby the cerebral blood flow is maintained at a constant level in spite of extreme factors tending to the contrary is discussed.

AUTHORS.

Edwards, Edward A.: Chronic Organic Arterial Disease. New England J. Med. 221: 251, 1939.

This is a review of the pathology, diagnosis, and treatment of peripheral arterial occlusion caused by arteriosclerosis and thromboangiitis obliterans. The author points out that a patient can never expect a return of perfect function in the affected limb since the collateral vessels, although they may equal in the aggregate the caliber of the blocked artery, cannot transmit the quantity of blood passing through the previously normal arteries. In the small collateral arteries the pulse wave is damped and the blood oozes through under a lowered pressure. This, however, does not diminish the importance of therapeutic attempts to increase blood flow through collateral vessels.

NAIDE.

Symposium on Heart Disease, American Roentgen Ray Society, Sept. 20, 1938.

1. **Hodges, Fred Jenner: Determination of Heart Size.** Am. J. Roentgenol. 42: 1, 1939.

Procedures designed to estimate cardiac size by roentgen methods are available but it does not follow that measurements of this sort can be made with great exactitude, nor is it true that exact heart size determination is essential to good diagnosis. It is one matter to attempt heart size measurements in selected normal individuals, quite another to attempt such procedures in the case of many individuals where knowledge regarding exact heart size may be of paramount importance to the clinician in determining the diagnosis or observing the effects of treatment. A great variety of situations commonly encountered by roentgenologists, contrive in one way or another to defeat attempts to provide accurate cardiac measurements.

The continued search by means of experimental and clinical observation for a truly accurate method of heart size determination during life will, and should go on. For, if this goal can be achieved, new fields of usefulness can be explored. The ambition of cardiologists to develop some reliable method of estimating cardiac reserve and thereby to evaluate with accuracy the disability produced by various cardiac lesions is a worthy one.

AUTHOR.

2. **Robb, George P., and Steinberg, Israel: Visualization of the Chambers of the Heart, the Pulmonary Circulation, and the Great Blood Vessels in Heart Disease.** Am. J. Roentgenol. 42: 14, 1939.

The results obtained by visualization of the chambers of the heart and the thoracic blood vessels in patients having rheumatic, syphilitic, hypertensive, and arteriosclerotic cardiovascular disease are reported and their value is discussed. Visualization in heart disease as in the normal gives a detailed picture of the cardiovascular system in which each major structure can be examined separately and its characteristics observed. As a result it has been possible to determine accurately the location and the degree of the gross pathologic changes, thereby providing a means of solving certain hitherto perplexing problems.

The prominence of the pulmonary arc in the frontal view in our patients with rheumatic mitral stenosis and insufficiency was caused directly by the dilated pulmonary artery and not by the enlarged pulmonary conus or the left atrium; the left auricula formed the convexity immediately below the pulmonary arch. Elevation of the left bronchus was not caused by the left atrium but apparently by engorged pulmonary veins. In syphilitic aortitis, the intracardiac portion of the aorta, the most frequent site of involvement and one previously invisible, was outlined and the exact size, shape, and location of aneurysms of the aorta was determined. The degree of left ventricular hypertrophy and dilatation, the tortuosity and unfolding of the thoracic aorta, the "buckling" of the innominate artery and the identity of the vessel forming the anterior boundary of the "aortic triangle" were demonstrated in hypertensive heart disease. In the patient with arteriosclerotic cardiovascular disease, the heart was found to be normal in size, the apparent enlargement in the conventional roentgenogram being due to the deviated spine, whereas the aorta exhibited a moderate degree of dilatation, elongation, and unfolding with calcification and thickening of the wall.

From these preliminary observations it seems apparent that inference regarding the condition of the heart which is based upon grossly indirect evidence such as the alteration of the cardiac silhouette and the disturbance of adjacent structures can now be largely replaced by exact information obtained by separate visualization of the four chambers of the heart and the great blood vessels. As a consequence, the interpretation of conventional roentgenoscopy and roentgenography will become more accurate, enhancing the value of these widely used clinical methods of examination and ultimately making visualization of the chambers of the heart and the thoracic blood vessels necessary only in cases presenting unusually difficult diagnostic problems.

AUTHORS.

3. Freedman, Eugene: Inflammatory Disease of the Pericardium. Am. J. Roentgenol. 42: 38, 1939.

Pericardial effusion leads to the formation of cardiac configurations which have been described by various authors as bag- or pear-shaped, or resembling a round bottle with a short neck. None of these configurations, however, are typical of pericardial effusion. They may be produced by decompensated hearts also. The best differential diagnostic sign between a decompensated heart and pericardial effusion is the one described by Holmes. This is based on the change of cardiac configuration during changes in the position of the patient. Unfortunately this procedure cannot be utilized in patients who are orthopneic. The kymographic examination may be helpful in differentiating pericardial effusions from decompensated hearts. Berner observed vigorous pulsations of the aortic knob and decreased pulsations of the left ventricular region on the kymogram of a patient suffering from pericardial effusion. After the effusion disappeared the kymographic recording of the pulsatory amplitude of the left ventricle and aortic knob became equal.

The recognition of early pericardial effusion may be facilitated by finding an abnormally convex bulging of the posterior surface of the heart either roentgenoscopically or on the lateral roentgenogram (Fleischner). The most reliable method is the daily roentgen examination of the heart and the finding of considerable change in its size within short periods of time. Kienböck's inflammatory diverticulum of the heart represents an encapsulated pericardial effusion, most commonly on the right border. The remaining part of the pericardial cavity is usually obliterated.

Cardiac compression due to pericardial scar formation is usually represented on roentgen examinations by a normal-sized or smaller than normal heart. Moderate or marked enlargement of the cardiopericardial shadow is uncommon and may be due either to an unusually marked thickening of the pericardium or to an underlying valvular or myocardial disease.

The majority of the compressed hearts are either triangular or, less commonly, globular. In rare instances a compressed heart may show a mitral or aortic configuration. The cardiac pulsations are usually diminished or absent. Occasionally, however, certain sections of the compressed heart may show vigorous pulsations. The aortic knob is flattened or completely obliterated in the majority of compressed hearts. Due to the marked thickening of the pericardium, the heart becomes rigid and in the majority of cases its configuration remains either unchanged or changes but little during the two phases of respiration. The adhesions between the heart and pericardium lead to a fixation of the heart. The degree of fixation is determined with the aid of expiratory and inspiratory posteroanterior roentgenograms taken with the patient lying on either side and with lateral views taken during both inspiration and expiration. The most conclusive sign of cardiac compression, the calcification of pericardium, is present only in the minority of instances (in nine among twenty-six patients). The kymographic examination is of no differential diagnostic value in cardiac compression. It only serves as a record which enables one to compare the difference between the pulsatory amplitude before and after removal of the pericardial scar.

AUTHOR.

4. Sosman, Merrill C.: Roentgenological Aspects of Acquired Valvular Heart Disease. Am. J. Roentgenol. **42**: 47, 1938.

Acquired valvular heart disease results in cardiac enlargement in almost every case and causes typical changes in the cardiac contour in the great majority.

Enlargement of the left auricle is one of the most reliable signs of mitral valvular disease.

The contour of the heart in aortic valvular disease may be duplicated by hypertensive heart disease but the differentiation can frequently be made by roentgenoscopy—in aortic regurgitation by the "rocking beat" and in aortic stenosis by demonstrating calcification in the aortic valve.

Calcification in aortic and mitral valves is frequently demonstrable roentgenoscopically and adds considerably to the accuracy in both structural and etiological diagnosis.

AUTHOR.

5. Levene, George: Roentgenologic Aspects of Non-Valvular Disease of the Heart. Am. J. Roentgenol. **42**: 60, 1939.

Nonvalvular disease of the heart and various forms of myocardial insufficiency frequently produce distinctive roentgenologic appearances. Careful roentgenologic study is therefore well suited to the identification and appraisal of disturbed cardiac dynamics. Its importance is further increased by its ability to depict the relationship of the greater and lesser circulation in the individual case. It offers confirmatory evidence of a diagnosis established by other clinical methods and frequently assists in the differentiation of the causes of cardiac enlargement and decompensation.

AUTHOR.

6. **Roesler, Hugo: Roentgenology of Congenital Cardiovascular Disease.** Am. J. Roentgenol. **42**: 72, 1939.

The author describes four groups of roentgenologic aspects of structural anomalies.

First, cases without any roentgenologic indication of the presence of defects; for example, the isolated interventricular septal defect of small size.

Second, deviations from the normal which are not characteristic for a congenital anomaly; for example, a general cardiac enlargement in the presence of a two- or three-chambered heart.

Third, certain conditions which reveal fairly characteristic features such as *coeur en sabot* or the large globular heart with marked enlargement of the pulmonary conus.

Fourth, structural anomalies with unequivocal roentgenologic findings.

McCULLOCH.

7. **Sussman, Marcy L.: Roentgen Examination of the Aorta and Pulmonary Artery.** Am. J. Roentgenol. **42**: 75, 1939.

Well-defined deviations from the normal in the size of the aorta yield evidence of disease. Methods of measurement do not permit of precise determination of minor deviations, particularly in the ascending portion. Experience in roentgenoscopy of the chest, particularly as it permits observation of the variations in the great vessels due to the position of the diaphragm, of posture, of chest deformity and of age, has appeared more valuable than rigid application of mensuration. The smaller the deviation from normal the less valuable and sometimes more confusing is the information obtained. The roentgen examination of the aorta may not prove particularly valuable in the early diagnosis of luetic aortitis. Pulmonary artery dilatation, when not due to a congenital anomaly, is not characteristic of any particular disease but is rather an expression of the state of the pulmonary circulation.

As regards the two great vessels, if the roentgen findings are considered alone and completely apart from the clinical data, the value of the examination has been overestimated in the literature. In actual practice it has its definite place when considered as an integral part of the physical examination.

AUTHOR.

Kerley, Peter: Intrathoracic Aneurysms. Brit. J. Radiol. **12**: 158, 1939.

This study is based on a series of sixty-two cases of intrathoracic aneurysms observed in Westminster and Royal Chest Hospitals, over a period of ten years, in whom the diagnosis was affirmed either by autopsy or by combined clinical, radiologic and pathologic investigations.

With good technique and careful consideration of the clinical and radiologic evidence, correct diagnosis can be achieved in 90 per cent of the cases. If kymography is available, the correct diagnosis can be made in 98 per cent of the cases. Mistakes occur in dissecting aneurysms where there is no obvious tumor, and in cases where the tumor is concealed by a collapsed lung.

AUTHOR.

Robb, George P., and Steinberg, Israel: Visualization of the Chambers of the Heart and the Thoracic Blood Vessels in Pulmonary Heart Disease: A Case Study. Ann. Int. Med. **13**: 12, 1939.

Detailed visualization of the cardiovascular system demonstrated for the first time during life the nature and the extent of the pathologic changes in pulmonary heart disease.

Cardiovascular mensuration may now become an exact procedure since it can measure fundamental anatomic structures rather than arbitrary diameters having no anatomical counterpart.

The recognition of the early stages of pulmonary heart disease which hitherto could not be diagnosed should now be possible.

AUTHORS.

Gross, Robert E., Emerson, Paul, and Green, Hyman: Surgical Exploration and Closure of a Patent Ductus Arteriosus. Surgery 6: 201, 1939.

A case is reported of an 11-year-old boy who had typical physical and x-ray findings of a patent ductus arteriosus. As the child had been followed over a period of several years, there had been slight but definite hypertrophy (or dilatation) of the heart, this change being presumably caused by the large shunt between the aorta and pulmonary artery. From statistical evidence, the boy presumably was facing a rather high probability of subsequent cardiac failure of some degree because of the burden imposed by the ductus shunt. Furthermore, this congenital lesion carried with it a high risk of subacute bacterial endocardial infection. In the attempt to reduce the work of the heart imposed by the shunt and also to lessen the danger of subacute bacterial endarteritis, surgical exploration was undertaken for obliterating the ductus. The vessel was found to be 11 to 12 mm. in diameter and was successfully ligated. The patient stood the operative procedure with extremely little reaction.

AUTHORS.

Laplace, Louis B.: Cardiovascular Complications of Fracture. Am. J. Surg. 44: 161, 1939.

Five hundred hospitalized cases of fracture were analyzed with respect to cardiovascular complications. The mortality for the cases having a normal cardiovascular system was 1 per cent; for those having associated cardiovascular disease, 34 per cent. The vast majority of fracture patients who died had clinical evidence of arteriosclerotic cardiovascular disease and had sustained a broken hip. Death resulted in these cases from a form of slowly progressive peripheral circulatory failure. The various ways in which fractures may cause damage or functional impairment of the cardiovascular system are discussed.

AUTHOR.

Allen, Frederick M.: Surgical Considerations of Temperature in Ligated Limbs. Am. J. Surg. 45: 459, 1939.

The survival limit of the leg tissues of several mammalian species, deprived of circulation, is increased by reduction of temperature of the environment surrounding the ischemic limbs. At room temperature the survival limit of the leg tissues is above fifteen hours. Above room temperature gangrene and systemic shock occur in less than fifteen hours. Near 0° C. recovery is possible after ligation for fifty-four hours.

The applications of refrigeration to surgery of ischemic legs is discussed. Of special interest is the suggestion that the period during which embolectomy may be performed successfully is much longer at ice temperature than at higher temperatures.

NAIDE.

Hill, R. M.: Vascular Anomalies of the Upper Limbs Associated With Cervical Ribs. Brit. J. Surg. **27**: 100, 1939.

A case is described of bilateral cervical ribs accompanied by vasomotor disturbances of the hands of the acrocyanosis type in which removal of a rib and fibromuscular band produced relief of pain, diminution of swelling, and improvement in the color changes of the hand on the corresponding side.

The symptoms of vasoconstriction were proved, at operation, to be caused by irritation of the lower trunk of the brachial plexus by the inner border of the cervical rib, a fibromuscular band and the scalenus anticus muscle.

NAIDE.

Blumgart, Herrman L., and Altschule, Mark D.: Should Digitalis Be Administered to Patients With Pre-existing Partial Heart Block? Am. J. M. Sc. **198**: 455, 1939.

In treating patients with pre-existing partial heart block, the physician is not infrequently confronted with the difficult decision as to whether digitalis should be prescribed, because of the danger of further interference with the passage of impulses on the one hand, and clear indications for its administration on the other. So far as we are aware, no suitable body of evidence bearing on this question is available.

Nineteen patients ranging in age from 15 to 72 years were studied. Congestive heart failure was present in almost all subjects. In 3, a varying 2-to-1 and 1-to-1 relationship between auricular and ventricular contractions existed. In most of the patients prolongation of the P-R interval was due to coronary sclerosis; in the others, rheumatic heart disease was present.

A standardized preparation of digitalis was administered in doses calculated on the basis of body weight; in accord with general practice, somewhat less than the full Eggleston dosage was administered.

The results demonstrate that digitalis in doses sufficient to induce therapeutic effects may be given to patients with partial heart block without causing interference with the orderly passage of impulses from the auricles to the ventricles. The dosages employed were those usually employed in treating patients with congestive failure in the hospital; the adequacy of the amounts used was indicated by the therapeutic response; it was not considered germane to this study to give amounts which would produce toxic manifestations, although in 6 cases nausea occurred without change in the P-R interval.

The results of this study show that while digitalis and organic heart disease each result in interference with auriculoventricular conduction, these factors do not reinforce each other, and their simultaneous presence does not lead to an additive effect when doses in therapeutic amounts such as were used in the present study are utilized. The presence of partial heart block does not constitute a contraindication to the use of digitalis.

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INDEX TO VOLUME 18

A

Abnormality, congenital, transposition of great cardiac vessels with special reference to phylogenetic theory of Spitzer, 635*
Abramson, David I., Zazeela, H., and Oppenheimer, B. S., 290
Acrocyanosis, effect of sleep on skin temperature in, 253*
Adrenaline (See suprarenal substance)
Adson, Alfred W., Kvale, W. F., and Allen, E. V., 537
Age, old, electrocardiogram in, 692
  sex and hypertension in, myocardial infarction due to coronary occlusion, 632*
Allen, Arthur C., 129*
Allen, Edgar V., and Kvale, W. F., 519, 546, 557
—, —, and Adson, A. W., 537
Allen, Frederick M., 772*
Altschule, Mark D., 1
—, and Blumgart, H. L., 773*
—, Gilligan, D. R., and Linenthal, A. J., 628*
American Heart Association, announcement, 132
    fifteenth scientific meeting, discussion of papers, 593
Amphetamine sulfate, effects, comparative of, paredrine and propadrine on blood pressure, 89
Andrus, E. Cowles, and Wilcox, H. B., Jr., 244*
Aneurysm, dissecting, of aorta, 67
  intrathoracic, 771*
  of popliteal artery, 471
    pulmonary artery, 562
    ventricle, electrocardiographic findings in, 630*
  ruptured, 471
Angina pectoris, caused by hematomyelia, 248*
    due to coronary artery disease, drug treatment of, 254*
    effect of oxygen on exercise tolerance of patients with, 150
    electrocardiogram, four lead of, new diagnostic features in, 128*
    electrocardiographic alterations after effort in normals and patients with, with special reference to chest leads, 245*
    glucose, hypertonic solution of, in, 411
Angina pectoris—Cont'd
    in hereditary xanthomatosis, 633*
    nerve pathways, physiology, symptomatology, and treatment, 640 (B. rev.)
    patient with, whose adrenals have been irradiated, tendency of electrocardiogram to become normal in, 639*
    value, diagnostic, of triphasic rapid wave in, and coronary syndrome, 246*
Anoxemia, experimental electrocardiographic changes in health and disease during, 257 (B. rev.)
Aorta, abdominal, effect on blood pressure of constriction of, above and below site of origin of both main renal arteries, 250*
    embolism and thrombosis of, 57
  aneurysm, dissecting of, 67
  chemoreceptors of, location and function of, 504*
  medionecrosis idiophatica cystica, of, 188
  roentgen examination of, and pulmonary artery, 771*
  transposition, complete, of, and pulmonary artery, 108
Aortitis, syphilitic, combined, and rheumatic disease of heart, 672
Arana, R., Castex, M. R., Ramirez, R. L., and Battro, A., 507*
Arrhythmia, sinus, in presence of extrasystole, 631*
    studies of, in patients with labile circulation, 247*
Arteriosclerosis, cerebral blood flow in, 767*
  diagnosis of, in lower extremities, oscillometry in, 506*
  infection, chronic, and, 380*
  obliterans, intermittent claudication due to, effect of deproteinated pancreatic extract in treatment of, 425
Artery, coronary, disease of, drug treatment of angina pectoris, 254*
    significance of duration of Q_3 with respect to, 308
    syndrome from, value, diagnostic, of a triphasic rapid wave in angina pectoris and, 246*
  embolism of, 747
  innervation of, observation on, of dog, 381*

*An asterisk (*) after a page number indicates the reference is an abstract and not an original article.

Artery, coronary—Cont'd
occluded, chronically, magnitude, adequacy, and source of collateral blood flow and pressure in, 513*
occlusion of, 633*
acute of, activities associated with onset of, 434
age, sex, and hypertension in, in myocardial infarction, due to, 632*
sudden of, reflex coronary artery spasm following, 632*
of dog, 403
spasm reflex of, following sudden occlusion of other coronary branches, 632*
thrombosis of, changes in chest lead electrocardiogram in, 636*
occurrence of, in polycythemia vera, 638*
disease, experimental of, effect of sympathectomy on, 251*
occlusive of, and hyperthyroidism, rate of circulation in arteries and veins in, 519
of leg, treatment of by Sander's vasocillator, 312
organic, chronic of, 768*
lesions produced in, of dogs, by injections of lipids, 373*
occlusion of, in left upper extremity of mongoloid idiot with congenital heart disease (tetralogy of Fallot), 241
popliteal, aneurysm, ruptured, of, 471
pulmonary, aneurysm of, 562
embolism of, cardiac sequelae of, 513*
is stellate infiltration in, justified? 124*
roentgen examination of aorta and, 771*
thrombosis of, capillary rupture with intimal hemorrhage as cause of, 451
transposition, complete, of aorta and, 108
Asthma, bronchial, differentiation of left ventricular failure from, by circulation time and other criteria, 765*
experimentally produced, in guinea pigs, electrocardiographic studies in, 247*
Atherosclerosis (*see* Arteriosclerosis)
Athletics, acute cardiac damage in healthy individuals following, 629*
Atlas, Lawrence N., 506*
Atropine, paroxysmal bundle branch block converted into two-to-one bundle branch block by means of, 115
Auricle, fibrillation, benign of, with repeated emboli, quinidine in treatment of, 494
clinical and experimental of, earliest correlation of, 684
of twenty-two months' duration with return to normal sinus mechanism without aid of quinidine, 102
relation between prolonged P-R interval and, in patients with rheumatic heart disease, 1
vagal and extravagal factors in cardiac slowing by digitalis in patients with, 374*
left, mammalian, rhythmicity and automatism in, 121*
strips of, from warm-blooded animals, is there a positive inotropic action of cholin derivatives on? 245*
tremulation of, 247*
Ayman, David, and Goldshine, A. D., 246*

B

Bailey, Robert L., and Stewart, H. J., 271*
Barker, Nelson W., and Roth, G. M., 312
Barnes, Arlie R., Burchell, H. B., and Mann, F. C., 133
Battro, A., Castex, M. R., Arana, R., and Ramirez, R. L., 507*
Bayley, Robert H., 308
Beck, William C., Scupham, G. W., de Takats, G., and Van Dellen, T. R., 504*
Bed, Sanders (*see* Vasocillator)
Bellet, Samuel, Gouley, B., Nichols, C. F., and McMillan, T. M., 483
Benzedrine (*see* Amphetamine)
Bile, whole, and bile salts, effects of, on perfused heart, 171
Bisgard, J. Dewey, 250*
Blahd, Margery, Frank, I., and Saphir, O., 248*
Block, Malcolm, 684
Blood, circulation of, control of, 256 (B. rev.)
flow of, peripheral disturbance of, 384 (B. rev.)
cerebral of, in arterial hypertension, arteriosclerosis and high intracranial pressure, 767*
collateral of, magnitude, adequacy, and source of, and pressure in chronically occluded coronary arteries, 513*
peripheral, of, effect of carbon dioxide inhalation on, in normal and in sympathectomized patient, 206
in man, plethysmographic studies of, effect of smoking upon vascular beds in hand, forearm, and foot, 290

Blood, flow—Cont'd
venous of, speed of, error in sodium cyanide method of determining, 557
pressure, differential, in lesser circulation of unanesthetized dog, 122*
effect on, comparative, of amphetamine sulfate, paredrine, and propadrine, on, 89
of constriction of abdominal aorta above and below site of origin of both main renal arteries, 250*
normal, range of, 635*
postural changes in, and pulse rate, effect of fever on, 46
reactivity of, to adrenaline in first two years of life, 628*
reading of, standardization of, 95
studies of, in infants, 130*
systolic, simple method for determining, in unanesthetized rat, 249*
vessels, anomalies of, of upper limbs associated with cervical ribs, 773*
great, clinical radiology of heart and, 516 (B. rev.)
visualization of, in heart disease, 768*
peripheral, organic disease of, testosterone propionate as therapeutic agent in patients with, 515*
thoracic, visualization of, in pulmonary heart disease, 771*
Blumenthal, Basil, and Oppenheimer, E. T., 363
Blumgart, Herrman L., and Altschule, M. D., 773*
—, Katzin, H. M., and Waller, J. V., 638*
de Boer, S., 375*
Bohning, Anne, Katz, L. N., Robinow, M., and Gertz, G., 25
Book review, Adventures in respiration, 258
Aktuelle Kreislauffragen, 641
Angina pectoris: nerve pathways, physiology, symptomatology, and treatment, 640
Atlas of clinical phonocardiography, 382
Cardiovascular disease in general practice, 383
Cardiovascular diseases, their diagnosis and treatment, 641
Clinical radiology of heart and great vessels, 516
Control of circulation of blood, 256
Electrocardiographic changes in health and disease during experimental anoxemia, 257
Elements of clinical physiology of the circulatory apparatus, 384
Book review—Cont'd
Peripheral disturbance of blood flow, 384
Peripheral vascular diseases, 517
Registration and interpretation of cardiac activity, 256
Rheumatic diseases of the circulation, 383
Symposium on the synapse, 642
The patient as a person, 643
Bouvrain, Yves, 251*
Boyd, Linn J., and McGavack, T. H., 562
—, and Scherf, D., 641
Boyer, Norman H., 115
Boyle, Robert W., McDonald, C. H., and DeGroat, A. F., 201
Brain disease, chronic rheumatic, as cause of mental disorders, 379*
Braun-Menendez, E., and Solari, L. A., 126*
Breathing, holding of, test, 246*
Brown, Morton G., and Riseman, J. E. F., 150
Brucer, Marshall, and Robinson, S. C., 635*
Bruetsch, Walter L., 378*, 379*
Bruger, Maurice, and Miller, J. H., 329
Buchbinder, William C., and Saphir, O., 510*
Burch, George E., 102
Burchell, Howard B., Barnes, A. R., and Mann, F. C., 133
Burger, R., 375*
—, and Wuhrmann, F., 376*
Burke, Mead, and Middleton, W. S., 634*

C

Calcium, synergism of, and digitalis, 505*
gluconate, measurement of circulation time with, in patients receiving digitalis, with electrocardiographic studies, 228
Calô, A., 382
Campbell, Maurice, and Elliot, G. A., 507*
Capillary, blood, character and distribution of, 248*
rupture of, with intimal hemorrhage as cause of pulmonary thrombosis, 451
Carbon dioxide, inhalation of, effect of, on peripheral blood flow in normal and sympathectomized patient, 206
use of, as test of circulation time, 374*
Cardiovascular system, changes in, in essential hypertension, with special reference to electrocardiogram in hypertension, 636*

Cardiovascular system—Cont'd
complications in, from fracture, 772*
disease of, 641 (B. rev.)
congenital of, roentgenology of, 771*
in general practice, 383 (B. rev.)
effect of fluid administered intravenously on, 628*
syphilis of, necropsy survey of, with particular reference to its decreasing incidence, 248*
Cash, James R., and Wood, J. E., Jr., 767*
Castaigne, J., and Dodel, P., 384*
Castex, M. R., Arana, R., Ramirez, R. L., and Battro, A., 507*
Ceylon, rheumatic heart disease as met with in hospital practice in, 766*
Chamberlain, E. Noble, and Hay, J. D., 377*
Chamberlain, F. L., Scudder, J., and Zwemer, R. L., 458
de la Chapelle, Clarence E., and Kossmann, C. E., 344, 352
Chasis, H., Smith, H. W., Rovenstine, E. A., Goldring, W., and Ranges, H. A., 253*
Childhood, heart disease, congenital in, with special reference to prognosis, 80
Children, cardiac enlargement in, with rheumatic heart disease, value of special radiologic procedures in detecting, 213
school, incidence of organic heart disease in, 705
Cholin, derivatives of, action, inotropic positive, of, is there a, on auricular strips from warm-blooded animals? 245*
Christianson, Oscar O., 373*
Circulation, coronary insufficiency, experimental, of, action of strophanthin in, 628*
electrocardiogram in, hemorrhage and reinfusion, 248*
disease, rheumatic, of, 383 (B. rev.)
increased, voluntary, 629*
peripheral, disturbance of, action of strophanthin in, 245*
pulmonary, visualization of, in heart disease, 768*
rate of, in arteries and veins of man in hypertension, of orthostatic hypotension, and of effect of sympathectomy, 537
of normal subjects and of those with occlusive arterial disease and hyperthyroidism, 519
readjustment of, during exercise, to that following adrenalin intravenously, resemblance in man of, 245*
Circulation—Cont'd
time of, differentiation of left ventricular failure from bronchial asthma by, and other criteria, 765*
measurement, with calcium gluconate in patients receiving digitalis, with electrocardiographic studies, 228
use of CO_2 inhalation as test of, 374*
Circulatory system, physiology, clinical, of, 384 (B. rev.)
Cirrhosis, cardiac, of liver, 638*
Cold-pressor reaction in normal subjects and in patients with primary (essential) and secondary (renal) hypertension, 329
Collens, William S., and Wilensky, N. D., 517
Comeau, Wilfrid J., and White, P. D., 334
Comroe, Julius H., Jr., 504*
Conduction defects, persistent, following diphtheria, 507*
time, delay in, relation between, and auricular fibrillation in patients with rheumatic heart disease, 1
Conductivity, relative of tissue in contact with heart, 244*
Contratto, A. W., Robinson, R. W., and Levine, S. A., 126*
Convallan, in cardiac therapy, 444
Cottenot, P., Laubry, C. H., Rositier, D., and Heim, R., 516
Cowan, John, 125*, 376
Crago, F. Hughes, and Spink, W. W., 515*
Cramer, H., and Schlomka, G., 631*
Crawford, J. Hamilton, and Gubner, R., 8
—, —, and Schnur, S., 374*
—, —, Smith, W. A., and Ungerleider, H. E., 729
Crynes, S. F., and Hunter, W. C., 635*
Cyanosis, infrared photographic demonstration of superficial venous pattern in congenital heart disease with, 282

D

Dack, Simon, Horn, H., and Friedberg, C. K., 513*
—, Master, A. M., and Jaffe, H. L., 254*, 434, 632*
Day, Richard, and Klingman, W. O., 253*
Death, sudden and unexpected, from acute interstitial myocarditis, 765*
DeGroat, A. F., Boyle, R. W., and McDonald, C. H., 201
Deepe, B., and Diefenhardt, H. H., 245*
Depropanex (*see* Pancreas, extract of)

Diabetes, coma from, systole in insulin shock and, 247*
Diet, alterations of cardiac minute volume by, 630*
Dietrich, Siegfried, 383
Digestion, influence of, on rate of circulation in arteries and veins of man, 546
Digitalis, patients receiving, measurement of circulation time with calcium gluconate in, with electrocardiographic studies, 228
should it be administered to patients with pre-existing partial heart block? 733*
synergism of calcium and, 505*
use of, in heart failure with normal rhythm, 130*
vagal and extravagal factors in cardiac slowing by, in patients with auricular fibrillation, 374*
a-N-dimethyl-p-hydroxyphenethylamine, mechanism of arterial hypertension induced by, 380*
Diphtheria, persistent conduction defect following, 507*
toxin of, effect of, upon heart, 201
Dodel, P., and Castaigne, J., 384*
Dow, Philip, and Hamilton, W. F., 122*, 125*
Dressen, M., and Schlomka, G., 632*
Drinker, Cecil K., 389
Dry, Thomas J., and Willius, F. A., 765*
Ductus arteriosus, patent, surgical exploration and closure of, 772*
Duntley, S. Quimby, Edwards, E. A., and Hamilton, J. B., 515*
Duryee, A. Wilbur, Fisher, M. M., and Wright, I. S., 425

E

East, Terrence, 383*
Edens, E., 639*
Edwards, Edward A., 768*
—, Hamilton, J. B., and Duntley, S. Q., 515*
Edwards, Joseph C., and Vander Veer, J. B., 127*
Effort, electrocardiographic alterations after, in normals and patients with angina pectoris, with special reference to chest lead, 245*
index, economy of, for heart of normal and hypertensive subjects, 123*
Electrocardiogram, alterations in, after effort, in normals and patients with angina pectoris, with special reference to chest lead, 245*
changes in, associated with experimental alterations in blood potassium in cats, 458
Electrocardiogram, changes—Cont'd
in health and disease during experimental anoxemia, 257 (B. rev.)
precordial leads, pathogenesis of bundle branch block as elucidated by, 509*
chest lead, changes in, in coronary thrombosis, 630*
multiple in man, value and significance of, 25
clinical significance of right axis deviation in, 334
findings in, in cases of ventricular aneurysm, 630*
four leads, new diagnostic features in, of angina pectoris, 128*
in aged, 692
in experimental coronary insufficiency, hemorrhage, and reinfusion, 248*
in hypertension, cardiovascular changes in essential hypertension with special reference to, 636*
in hyperthyroidism, 632*
in single and double ovum twins, 631*
interpretation of calcareous stenosis of aortic valve, 765*
leads, precordial of, form of, effect of posture on, 271
measurement of circulation time with calcium gluconate in patients receiving digitalis, by, 228
normal, 377*
of dog, after phlorrhizin poisoning, 245*
picture of, of experimental localized pericarditis, 133
precordial, in myocardial infarction, in diffuse lesions, 352
in infarction of posterior wall of left ventricle, 344
lead, 126*
prognosis by, 631*
relation between prolonged P-R interval and auricular fibrillation in patients with rheumatic heart disease, 1
researches in, 375*
significance of duration of Q_3 with respect to coronary disease, 308
showing "second positive wave of QRS" in Lead III, 377*
small and absent initial positive deflections in chest lead, 127*
strophanthin, 247*
studies by, in experimentally produced asthma in guinea pigs, 247*
T wave of, and potassium, 246*
tendency of, to become normal in angina pectoris patients whose adrenals have been irradiated, 639*
triphasic rapid wave of, diagnostic value of, in angina pectoris and coronary syndrome, 246*

Electrocardiogram—Cont'd
ventricular, complexes, variform of, ventricular tachycardias with, 124*
Electrocardiography, clinical, chest leads in, 125*
Electrode, precordial, new, 94
Eliaser, Maurice, Jr., and Konigsberg, J., 630*
Elliot, G. A., and Campbell, M., 507*
Embolism (*see* organ affected)
Emerson, Paul, Gross, R. E., and Green, H., 772*
Endocarditis, acute in wild animals with especial reference to opossum, 166
bacterial, due to streptococcus fecalis, 753
mechanism of localization of vegetations of, 129*
subacute, and chronic verrucose rheumatic, histopathology of psychoses with, 378*
caused by type XVIII pneumococcus, 500
evaluation of sulfanilamide in treatment of patients with, 515*
heart failure in, 510*
incidence and pathogenesis of myocardial lesions in, 766*
experimental, in dogs, 248*
streptococcus viridans, clinical-pathologic analysis of experience in Wisconsin General Hospital, 634*
England, Albert C., Jr., Harris, A. W., and Rosenbaum, F. F., 759
Epstein, Bernard S., 282
Esler, James Wallace (Memorial), 120
Essex, Hiram E., Wakim, K. G., and Mann, F. C., 171
Evans, Courtenay, 630*
Ewert, B., and Kallos, P., 247*
Exercise, influence of, on cardiac output in congestive heart failure, 252*
on rate of circulation in arteries and veins of man, 546
lactic acid production during rest and after, in subjects with various types of heart disease, with special reference to congenital heart disease, 374*
tolerance for, effect of oxygen on, of patients with angina pectoris, 150
Extrasystoles (*see* Heart, ectopic contractions)

F

Farber, Sidney, and Harris, J. S., 635*
Fasciolo, J. C., Houssay, B. A., and Taquini, A. C., 249*
Fernando, P. B., 766*
Fever, effect of, on postural changes in blood pressure and pulse rate, 46
Fisher, Martin M., Duryee, A. W., and Wright, I. S., 425
Fistula, arteriovenous, of lung, associated with polycythemia vera, 589
Flaxman, Nathan, and Volini, I. F., 510*
Flothow, Paul G., 514*
Fluids, administered intravenously, effect of, in cardiovascular system of man, 628*
Fontaine, René, Leriche, R., and Friedmann, L., 124*
Fox, Herbert, 166
Fox, Theodore, Gold, H., Kwit, N. T., and Otto, H., 374*
Fracture, cardiovascular complications of, 772*
Frank, Ira, Blahd, M., and Saphir, O., 248*
Freedman, Eugene, 769*
Frey, W., and Hadorn, W., 247*
Friedberg, Charles K., Horn, H., and Dack, S., 513*
Friedell, H. L., and Keys, A., 505*
Friedmann, Leon, Leriche, R., and Fontaine, R., 124*
Fry, Franklin W., 57

G

Garvin, Curtis F., and Work, J. L., 747
Gavey, C. J., and Parkinson, J., 130*
Geiger, Arthur J., 715
Gellhorn, Ernst, and Steck, I. E., 206
German Society for Study of Circulation, Transactions, 503*
Gertz, G., Bohning, A., Katz, L. N., and Robinow, M., 25
Gilligan, D. Rourke, Altschule, M. D., and Linenthal, A. J., 628*
Glucose, hypertonic solution of, in angina pectoris, 411
Goiter, intrathoracic, simulating right-sided cardiac enlargement, 237
Gold, Harry, Kwit, N. T., Otto, H., and Fox, T., 374*
Goldblatt, Harry, Kahn, J. R., and Hanzal, R. F., 250*
Goldman, Fred, McGuire, J., Shore, R., and Hauenstein, V., 252*
Goldring, W., Smith, H. W., Rovenstine, E. A., Chasis, H., and Ranges, H. A., 253*
Goldshine, Archis D., and Ayman, D., 246*
Goltman, David W., and Stern, N. S., 176
Gouley, Benjamin, Bellet, S., Nichols, C. F., and McMillan, T. M., 483
Graf, L., 631*
Graybiel, Ashton, and White, P. D., 122*
Green, Hyman, Gross, R. L., and Emerson, P., 772*
Gregg, Donald E., Thornton, J. J., and Mautz, F. R., 513*

Grollman, A., Williams, J. R., Jr., and Harrison, T. R., 249*
Gross, Harry, and Handler, B. J., 379*
Gross, Robert E., Emerson, P., and Green, H., 772*
Gubner, Richard, and Crawford, J. H., 8
—, —, Smith, W. A., and Ungerleider, H. E., 729
—, Schnur, S., and Crawford, J. H., 374*

H

Hadorn, W., and Frey, W., 247*
Hall, G. E., Manning, G. W., and McEarchern, C. G., 632*
Hallaran, W. R., Wright, G. W., and Wiggers, C. J., 123*
Hallock, Phillip, 374*
Halpern, S. Sherman, and Perlow, S., 381*
Hamilton, James B., Edwards, E. A., and Duntley, S. Q., 515*
Hamilton, W. F., and Dow, P., 121*, 122*
—, Woodbury, R. A., and Robinow, M., 130*
—, —, and Vogt, E., 122*
Handler, Bernard J., and Gross, H., 379*
Hanzal, Ramon F., Goldblatt, H., and Kahn, J. R., 250*
Harris, Alfred W., Rosenbaum, F. F., and England, A. C., Jr., 759
Harris, Jerome S., and Farber, S., 635*
Harrison, C. V., 251*
Harrison, Tinsley R., Williams, J. R., Jr., and Grollman, A., 249*
Hartog, H. S. Ph., Van Nieuwenhuisen, C. L. C., and Matthijssen, E., 128*
Hauenstein, Virgil, McGuire, J., Shore, R., and Goldman, F., 252*
Hay, J. Duncan, and Chamberlain, E. N., 377*
Healing, speed of, of myocardial infarction, 647
Heart, activity of, registration and interpretation of, 256 (B. rev.)
block, bundle branch, location of, 247*
paroxysmal, converted into two-to-one bundle branch block by means of atropine, 115
pathogenesis of, as elucidated by electrocardiographic changes in precordial lead, 509*
ventricular asynchronism in, 126*
intraventricular, prognosis of, 145
partial, pre-existing, should digitalis be administered to patients with? 773*
chambers of, visualization of, in heart disease, 768*
in pulmonary heart disease, 771*
Heart—Cont'd
contraction of, physiologic irregularities of, XI. Respiratory variations of Q_3, 632*
ectopic of, Q-T interval following, 631*
sinus arrhythmia in presence of, 631*
damage, acute, in healthy individuals following athletics, 629*
dilatation, tonogenic of, following increased venous return, 628*
disease of, congenital, of, 176
in childhood with special reference to prognosis, 80
lactic acid production during rest and after exercise in subjects with various types of heart disease with special reference to, 374*
(tetralogy of Fallot) arterial occlusion in left upper extremity of mongoloid idiot with, 241
with cyanosis, infrared photographic demonstration of superficial venous pattern in, 282
non-valvular of, roentgenologic aspect of, 770*
organic of, cardiac neurosis associated with, 153
incidence in school children, 705
pulmonary of, visualization of chambers of heart and thoracic blood vessels in, 771*
review of significant contributions made during 1938, 122*
rheumatic of, as met with in hospital practice in Ceylon, 766*
children with, value of special radiologic procedures in detecting cardiac enlargement in, 213
combined syphilitic aortitis and, 672
relation between prolonged P-R interval and auricular fibrillation in patients with, 1
valvular, acquired, roentgenologic aspects of, 770*
visualization of chambers of heart, pulmonary circulation, and great blood vessels in, 768*
effect of diphtheria toxin upon, 201
enlargement of, right-sided intrathoracic goiter simulating, 237
value of special radiologic procedures in detecting, in children with rheumatic heart disease, 213
failure of,
asthmatoid, a form of left ventricular failure and its differentiation from bronchial asthma by circulation time and other criteria, 765*

Heart, failure—Cont'd
congestive, influence of exercise on cardiac output in, 252*
chronic of, sclerosis of superior vena cava in, 379*
hyperpnea in, 375*
in subacute bacterial endocarditis, 510*
with normal rhythm, digitalis in, 130*
field, electrical of, 375*, 376*
function of, abnormalities in, studies on estimation of cardiac output in man, and of, 506*
human, significance of myocardial scars, 766*
stroke volume of, measurement of, from roentgenograms; simultaneous roentgenkymographic and acetylene rebreathing experiments, 505*
hypertrophy, experimental athlete, of, development and recession of, 121*
mechanism of, in a fatal case of acute thyrotoxicosis, 759
metastasis to, from malignant melanoma, 579
minute volume of, alterations of, by diet, 630*
murmur, auricular, of, factors influencing, and the intensity of the first heart sound, 261
loud, musical, diastolic of, of aortic insufficiency, 483
muscle, of, (*see* Myocardium)
neurosis of, associated with organic heart disease, 153
output of, influence of exercise on, in congestive heart failure, 252*
studies on estimation of, in man and of abnormalities in cardiac function, 506*
perfused, effect of whole bile and bile salts on, 171
radiology, clinical of, and great vessels, 516 (B. rev.)
revascularization, surgical of, 514*
roentgenkymography of, its clinical applications and limitations, 729
rhythm of, disturbances of, 125*, 376*
size of, determinations of, 768*
slowing of, by digitalis, vagal and extravagal factors in, in patients with auricular fibrillation, 374*
sounds of, first, intensity of, factors influencing auricular murmur and, 261
in young adults, 303
systole of, in insulin shock, and diabetic coma, 247*
tissues in contact with, relative conductivity of, 244*
Hegglen, R., 247*
Heim, R., Laubry, C. H., Cottenot, P., and Rositier, D., 516
Helwig, Ferdinand C., and Wilhelmy, E. W., 765*
Hematomyelia, angina pectoris caused by, 248*
Hemorrhage, intimal, capillary rupture with, as cause of pulmonary thrombosis, 457
Henderson, Yandell, 258
Herles, F., Lukl, P., Prusik, B., and Sikl, H., 247*
Heuer, George J., and Stewart, H. J., 129*
Hill, R. M., 773*
Hodges, Fred Jenner, 768*
Hoff, Hebbel E., Smith, P. K., and Winkler, A. W., 505*
Horn, Henry, Dack, S., and Friedberg, C. K., 513*
Horton, Bayard T., and Smith, H. L., 589
Houssay, B. A., Fasciolo, J. C., and Taquini, A. C., 249*
Hunter, Warren C., and Crynes, S. F., 635*
Hyperemia, reaction, quantitative relation between and myocardial ischemia which it follows, 373*
Hyperpnea in heart failure, 375*
Hypertension, age, sex and, in myocardial infarction due to coronary occlusion, 632*
arterial, cerebral blood flow in, 767*
mechanism of, induced by paredrinal (a-N-dimethyl-p-hydroxyphenethylamine), 380*
of renal origin, 240*
pathogenesis of, with special regard to role of kidney and adrenals in mechanism of white high blood pressure, 511*
comparison of, in athletes and nonathletes, 251*
electrocardiogram in, cardiovascular changes in essential hypertension with special reference to, 636*
essential, and secondary (renal), cold-pressor reaction in normal subjects and in patients with, 329
cardiovascular changes in, with special reference to electrocardiogram in hypertension, 636*
effect of non-specific operations in, 510*
surgical treatment of, 514*
experimental, studies on, effect on blood pressure of constriction of abdominal aorta above and below site of origin of both main renal arteries, 250*
obesity and, 767*

Hypertension—Cont'd
rate of circulation in arteries and veins in, 537
relation of hyperthyroidism to, 250*
urologic, 511*
Hyperthyroidism, acute (thyrotoxicosis), cardiac mechanism in, 759*
electrocardiogram in, 632*
relation of, to hypertension, 250*
Hypotension, orthostatic, rate of circulation in arteries and veins in, 537
postural, transient paralysis from, 637*

I

Idiot, mongoloid, with congenital disease (tetralogy of Fallot), arterial occlusion in left upper extremity of, 241
Infant, blood pressure studies on, 130*
Infarction (*see* organ affected)
Infection, chronic, and atherosclerosis, 380*
Insulin, shock from, systole in, and diabetic coma, 247*
Intermittent claudication due to arteriosclerosis obliterans treatment of, effect of deproteinated pancreatic extract, 425
Ischemia, myocardial, quantitative relation between reactive hyperemia and, 373*

J

Jaffe, Harry L., Master, A. M., and Dack, S., 254*, 434, 632*
Jochim, K., and Katz, L. N., 381*
Jones, Noble W., and Rogers, A. L., 380*
Joseph, N. R., Starr, I., Rawson, A. J., and Schroeder, H. A., 506*

K

Kahn, Joseph R., Goldblatt, H., and Hanzal, R. F., 250*
Kallos, P., and Ewert, B., 247*
Kaplan, L. G., and Katz, L. N., 145*
Katz, Louis N., Bohning, A., Robinow, M., and Gertz, G., 25
—, and Jochim, K., 381*
—, and Kaplan, L. G., 145
—, and Lindner, E., 244*, 373*
Katzin, Herbert M., Waller, J. V., and Blumgart, H. L., 638*
Kerley, Peter, 771*
Keys, Ancel, and Friedell, H. L., 505*
Kirch, E., and Nürmberger, W., 121*
Kisch, Franz, and Scherf, D., 124*
Klingman, Walter O., and Day, R., 253*
Konigs, G., and Schlomka, G., 124*
Konigsberg, Jerome, and Eliaser, M., Jr., 630*
Kopp, Israel, 46
Korth, C., and Sprang, K., 632*
Kossmann, Charles E., and de la Chapelle, C. E., 344, 352
Kramer, David W., 255*
Krause, M., and Mainzer, F., 245*
Kunkel, Paul, and Stead, E. A., Jr., 261, 380*
Kuttner, Ann G., and Reyersbach, G., 213
Kvale, Walter F., and Allen, E. V., 519, 546, 557
—, —, and Adson, A. W., 537
Kwit, Nathaniel T., Gold, H., Otto, H., and Fox, T., 374*

L

Lactic acid, production of, during rest and after exercise in subjects with various types of heart disease, with special reference to congenital heart disease, 374*
Laplace, Louis B., 772*
Larsen, Kaj H., 257
Latzel, M., 124*
Laubry, C. H., Cottenot, P., Rositier, D., and Heim, R., 516
Laubry, Charles, Soulie, P., and Laubry, P., 246*
Laubry, P., Laubry, C., and Soulie, P., 246*
Leads, chest, changes in, in coronary thrombosis, 630*
electrocardiographic alterations after effort in normals and patients with angina pectoris, with special reference to, 245*
IV R and IV F, comparative study of, 715
in clinical electrocardiography, 125*
multiple, value and significance of, in man, 25
significance of small and absent initial positive deflections in, 127*
precordial, 126*
pathogenesis of bundle branch block as elucidated by electrocardiographic changes in, 509*
Leary, Olga C., and Lia, B. R., 108
Leger, Lee H., and Major, R. H., 444
Lennox, William G., and Williams, D., 767*
Lepeschkin, E. W., 248*
Leriche, René, Fontaine, R., and Friedmann, L., 124*
Levene, George, 770*
Levine, Samuel A., Robinson, R. W., and Contratto, A. W., 126*
Levinsohn, Sandor A., and Wolf, I. J., 241
Levitt, George, 692
Lia, Bianca R., and Leary, O. C., 108
Lian, C., and Pinchenzon, B., 247*
Lindner, E., and Katz, L. N., 244*, 373*
Linenthal, Arthur J., Gilligan, D. R., and Altschule, M. D., 628*
Lipids, injection of, lesions produced in arteries of dogs by, 373*

Loman, Julius, Rinkel, M., and Myerson, A., 89
Lowell, T. C., 766*
Lukl, P., Herles F., Prusik, B., and Sikl, H., 247*
Lymph, formation and movement of, 389

M

Maher, C. C., and Wosika, P. H., 511*
Mainzer, F., and Krause, M., 245*
Maitra, J. M., 633*
Major, Ralph H., and Leger, L. H., 444
Malcomson, G. E., McDowell, R. J. S., and McWhan, I., 256
Mallory, G. Kenneth, White, P. D., and Salcedo-Salgar, J., 647
Mann, Frank C., Burchell, H. B., and Barnes, A. R., 133
—, Wakim, K. G., and Essex, H. E., 171
Manning, G. W., McEarchern, C. G., and Hall, G. E., 632*
Marx, L., 631*
Master, Arthur M., Dack, S., and Jaffe, H. L., 254*, 434, 632*
Matthijssen, E., Van Nieuwenhuisen, C. L. C., and Hartog, H. S. Ph., 128*
Mautz, Frederick R., Gregg, D. E., and Thornton, J. J., 513*
McDonald, C. H., Boyle, R. W., and DeGroat, A. F., 201
McDowell, R. J. S., Malcomson, G. E., and McWhan, I., 256
McEarchern, C. G., Manning, G. W., and Hall, G. E., 632*
McGavack, Thomas H., and Boyd, L. J., 562
McGuire, Johnson, Shore, R., Hauenstein, V., and Goldman, F., 252*
McMichael, John, 375*
McMillan, Thomas M., Bellet, S., Gouley, B., and Nichols, C. F., 483
McWhan, I., McDowell, R. J. S., and Malcomson, G. E., 256
Melanoma, malignant, cardiac metastasis from, 579
Meningococcus, pericarditis with effusion due to, 368
Mental disease, cause of, chronic rheumatic brain disease as, 379*
Middleton, William S., and Burke, M., 634*
Miller, H. R., 638,* 640
Miller, John H., and Bruger, M., 329
Mönks, L., 628*
Moragues, V., 579
Mortensen, Vagn, 509*
Mufson, Isidor, Mulinos, M. G., and Shulman, I., 255*
Mulinos, Michael G., Shulman, I., and Mufson, I., 255*
Müller, Carl, 633*
Myerson, Abraham, Loman, J., and Rinkel, M., 89
Myocarditis, interstitial, acute, sudden and unexpected death from, 765*
Myocardium, disease of, relative duration of systole in, 124*
infarction of, due to coronary occlusion, age, sex, and hypertension in, 632*
precordial electrocardiograms in, in cases of infarction of posterior wall of left ventricle, 344
in cases of diffuse lesions, 352
roentgenkymographic studies of, 8
speed of healing of, 647
ischemia of, quantitative relation between reactive hyperemia and, 373*
lesions of, incidence and pathogenesis of, in subacute bacterial endocarditis, 766*
scars in, significance of, in human heart, 766*

N

Naide, Myer, 254*
de Navasquez, S., 766*
Neuking, P., and Schlomka, G., 247*
Nicotinic acid, action on peripheral vascular system, 697
Nürmberger, W., and Kirch, E., 121*

O

Obesity and hypertension, 767*
evaluation of relative duration of systole in, 629*
Ogden, Eric, and Schock, N. W., 629*
Opossum, endocarditis, acute, in wild animals, with especial reference to, 166
Oppenheimer, B. S., Abramson, D. I., and Zazeela, H., 290
Oppenheimer, Enid Tribe, and Blumenthal, B., 363
Opsahl, Roald, 511*
Orgain, Edward S., and Poston, M. A., 368
Orías, Oscar, 256
Oscillometry in diagnosis of arteriosclerosis of lower extremities, 506*
O'Shaughnessy, Lawrence, Slome, D., and Watson, F., 514*
Osterwald, H., 628*
Otto, Harold, Gold, H., Kwit, N. T., and Fox, T., 374*
Oxygen, effect of, on exercise tolerance of patients with angina pectoris, 150

P

Pain, relief surgical of, due to circulatory disturbances of feet, 381*
rest, of ischemic origin, use of vitamin B_1 in, 254*

Pancreas, extract, deproteinated, of I effect in treatment of intermittent claudication due to arteriosclerosis obliterans, 425
Papaverin, treatment of Raynaud's disease with, intravenously, 255*
Paredrine, effect, comparative of, amphetamine sulfate, and propadrine on blood pressure, 89
Paredrinol (a-N-dimethyl-p-hydroxyphenethylamine), 380*
Parkinson, John, and Gavey, C. D., 130*
Paterson, J. C., 451
Patient as a person, 643 (B. rev.)
Peel, A. A. Fitzgerald, 377*
Pericarditis, constrictive, chronic, 129*
localized, experimental electrocardiographic picture of, 133
with effusion due to meningococcus, 368
Pericardium, disease, inflammatory of, 769*
rupture, traumatic of, 635*
Perlow, Samuel, and Halpern, S. S., 381*
Perry, C. Bruce, 507*
Phlorrhizin, poisoning by, electrocardiogram of dog after, 245*
Phonocardiography clinical, atlas of, 382 (B. rev.)
Photography, infrared, demonstration of superficial venous pattern in congenital heart disease with cyanosis, 282
Phylogenetic, theory of Spitzer, transposition of great cardiac vessels with special reference to, 635*
Pianetto, M. Besso, 403
Pinchenzon, B., and Lian, C., 247*
Plenczner, A., 251*
Plethysmogram, studies of peripheral blood flow in man, III effect of smoking upon vascular beds in hand, forearm, and feet, 290
Plotz, Milton, 765*
Pneumococcus, type XVIII, subacute bacterial endocarditis caused by, 500
Polycythemia vera, arteriovenous fistula of lung associated with, 589
occurrence of coronary artery thrombosis in, 638*
Popkin, Roy J., 697
Poston, Mary A., and Orgain, E. S., 368
Posture, changes in, effect of fever on, in blood pressure and pulse rate, 46
effect of, on form of precordial lead of electrocardiogram, 271
influence of on rate of circulation in arteries and veins of man, 546
Potassium, alterations, experimental of in blood in cats, electrocardiographic changes associated with, 458
and T wave of electrocardiogram, 246*
Propadrine, effect, comparative of, amphetamine sulfate, paredrine and, on blood pressure, 89
Prusik, B., Herles, F. Lukl, P., and Sikl, H., 247*
Psychosis, histopathology of, with subacute bacterial and chronic verrucose rheumatic endocarditis, 378*
Puddur, V., 245*
Pulse, rate, postural changes in blood pressure and, effect of fever on, 46
wave of, velocity of, experimental study of, propagated through aorta, 122*
standing of, experimental study of, propagated through aorta, 121*

Q

Quinidine, in treatment of benign auricular fibrillation with repeated emboli, 494
Q-T, interval following extrasystoles, 631*
Q wave, variations, respiratory of, 632*

R

Rabb, W., and Schönbrunner, E., 639*
Radiology (*see* also roentgenology)
Radványi, Géza, 631*
Rakov, Harold L., 500
Ramirez, R. L., Castex, M. R., Arana, R., and Battro, A., 507*
Ranges, H. A., Smith, H. W., Rovenstine, E. A., Goldring, W., and Chasis, H., 253*
Rasmussen, Hakon, and Thingstad, R., 636*
Rate of circulation in arteries and veins of man, error in sodium cyanide method of determining speed of venous blood flow, 557
Influence of temperature of skin, digestion, posture, and exercise, 546
Ratschow, M., 384
Rauh, Louise W., 705
Rawson, A. J., Starr, I., Schroeder, H. A., and Joseph, N. R., 506*
Raynaud's disease, treatment of, with papaverine intravenously, 255*
Respiration, adventures in, 258 (B. rev.)
study of, in cardiacs, contribution to, 251*

Rest, lactic acid production during, and after exercise in subjects with various types of heart disease, with special reference to congenital heart disease, 374*
Reyersbach, Gertrude, and Kuttner, A. G., 213
Ribs, cervical, vascular anomalies of upper limbs associated with, 773*
Rinehart, James F., and Soley, M. H., 237
Rinkel, Max, Loman, J., and Myerson, A., 89
Riseman, Joseph E. F., and Brown, M. G., 150
Robb, George P., and Steinberg, I., 768,* 771*
Robert, John Thomas, 188
Roberts, Ralph C., and Sacks, H. A., 303
Robinow, M., Bohning, A., Katz, L. N., and Gertz, G., 25
—, Woodbury, R. A., and Hamilton, W. F., 130*
Robinson, G. Canby, 643
Robinson, Roger W., Contratto, A. W., and Levine, S. A., 126*
Robinson, Samuel G., and Brucer, M., 635*
Roemheld, L., 630*
Roentgenkymogram, of heart, its clinical application and limitations, 729
studies by, of myocardial infarction, 8
Roentgenogram, aspects of acquired valvular heart disease, 770*
congenital cardiovascular disease, 771*
nonvalvular disease of heart, 770*
examination of aorta and pulmonary artery, 771*
measurement of stroke volume of human heart from, 505*
value of, special procedures in detecting cardiac enlargement in children with rheumatic heart disease, 213
Roentgenology, clinical of heart, and great vessels, 516 (B. rev.)
Roesler, Hugo, 771*
Rogers, Arthur L., and Jones, H. W., 380*
Rogers, Hobart, 67
Rosenbaum, Francis F., Harris, A. W., and England, A. C., Jr., 759
Rositier, D., Laubry, C. H., Cottenot, P., and Heim, R., 516
Roth, Grace M., and Barker, N. W., 312
Rothberger, C. J., and Sachs, A., 121,* 245*
Rovenstine, E. A., Smith, H. W., Goldring, W., Chasis, H., and Ranges, H. A., 253*

S

Sachs, Arpad, and Rothberger, C. J., 121,* 245*
Sacks, Herbert A., and Roberts, R. C., 303
Salcedo-Salgar, Jorge, Mallory, G. K., and White, P. D., 647
Saphir, Otto, Blahd, M., and Frank I., 248*
—, and Buchbinder, W. C., 510*
Scherf, David, and Boyd, L. J., 641
—, and Kisch, F., 124*
—, and Weissberg, J., 411
Schleicher, I., 629*
Schlomka, G., and Cramer, H., 631*
—, and Dressen, M., 632*
—, and Konigs, G., 124*
—, and Neuking, P., 247*
—, and Witsch, F., 629*
Schnur, Sidney, 153
—, Gubner, R., and Crawford, J. H., 374*
Schönbrunner, E., and Rabb, W., 639*
Schroeder, H. A., Starr, I., Rawson, A. J., and Joseph, N. R., 506*
Scudder, J., Chamberlain, F. L., and Zwemer, R. L., 458
Scupham, George W., de Takats, G., VanDellen, T. R., and Beck, W. C., 504*
Selzer, A., and Wood, P., 125,* 378*
Sex, age, and hypertension in myocardial infarction due to coronary occlusion, 632*
Schock, N. W., and Ogden, E., 629*
Shore, Rose, McGuire, J., Hauenstein, V., and Goldman, F., 252*
Shulman, Israel, Mulinos, M. G., and Mufson, I., 255*
Sikl, H., Herles, F., Lukl, P., and Prusik, B., 247*
Skin, temperature of, effect of sleep on, in acrocyanosis, 253*
influence of, on rate of circulation in arteries and veins of man, 546
Sleep, effect of, on skin temperature in acrocyanosis, 253*
Slome, David, O'Shaughnessy, L., and Watson, F., 514*
Smith, Harry L., and Horton, B. T., 589
Smith, H. W., Rovenstine, E. A., Goldring, W., Chasis, H., and Ranges, H. A., 253*
Smith, Paul K., Winkler, A. W., and Hoff, H. E., 505*
Smith, Wilbur A., Gubner R., Crawford, J. H., and Ungerleider, H. E., 729
Smoking, (*see* tobacco)
Sodium cyanide, error in method of, of determining speed of venous blood flow, 557
Sokolow, Maurice, 494
Solari, L. A., and Braun-Menedez, E., 126*

Soley, Mayo H., and Rinehart, J. F., 237
Soloff, Louis A., 318
Sosman, Merrill C., 770*
Soulie, P., Laubry, C., and Laubry, P., 246*
Spang, K., and Korth, C., 632*
Spink, Wesley W., and Crago, F. H., 515*
Sprenger, O., 503*
Starr, Isaac, Rawson, A. J., Schroeder, H. A., and Joseph, N. R., 506*
Stead, Eugene A., Jr., and Kunkel, P., 261, 380*
Steck, Irving E., and Gellhorn, E., 206
Steinberg, Israel, and Robb, G. P., 768*, 771*
Stern, Newton S., and Goltman, D. W., 176
Stewart, Harold J., and Bailey, R. L., 271
—, and Heuer, G. J., 129*
Streptococcus fecalis, bacterial endocarditis due to, 753
Strophanthin, action of, in peripheral circulatory disturbance, 245*
in experimental coronary insufficiency, 628*
indirect and direct, 639*
electrocardiogram from, 247*
Sulfanilamide, evaluation of, in treatment of patients with subacute bacterial endocarditis, 515*
Suprarenal substance, reactivity of blood pressure to, in first two years of life, 628*
resemblance in man of circulatory readjustment during exercise to that following, 245*
Sussman, Marcy L., 771*
Swanson, Homer, 672
Sympathectomy, effect of, on rate of circulation in arteries and veins, 537
on development of experimental arterial disease, 251*
patients with, effect of carbon dioxide inhalation on peripheral blood flow in normal and in, 206
Synapse, symposium on, 642 (B. rev.)
Syphilis, cardiovascular necropsy survey of, with particular reference to its decreasing incidence, 248*
Systole, duration, relative of, evaluation of, in obese people, 629*
in heart muscle disease, 124*
in hot baths, 124*
Stellate ganglion, infiltration of, in pulmonary embolism, is it justified? 124*

T

Tachycardia paroxysmal, etiology and prognosis, 507*
ventricular, paroxysmal, 507*
de Takats, Géza, Scupham, G. W., Van Dellen, T. R., and Beck, W. C., 504*
Taquini, A. C., Houssay, B. A., and Fasciolo, J. C., 249*
Temperature, of ligated limbs, surgical considerations of, 772*
Testosterone propionate, as therapeutic agent in patients with organic disease of peripheral vessels, 515*
Thiele, G., 628*
Thingstad, Rolv, and Rasmussen, H., 636*
Thomas, Henry M., Jr., 637*
Thomson, W. A. R., 246*
Thornton, John J., Gregg, D. E., and Mautz, F. R., 513*
Thrombosis (*see* organ affected)
Thyrotoxicosis, (*see* hyperthyroidism)
Tobacco, effect of smoking upon vascular bed in hand, forearm, and foot, 290
Twins, single and double ovum, electrocardiogram in, 631*

U

Ungerleider, Harry E., Gubner, R., Crawford, J. H., and Smith, W. A., 729

V

Valve, aortic, insufficiency of, loud musical diastolic murmurs of, 483
stenosis, calcareous, of, interpretation of electrocardiographic findings in, 765*
Van Dellen, Theodore R., Scupham, G. W., de Takats, G., and Beck, W. C., 504*
Vander Veer, Joseph B., and Edwards, J. C., 127*
Van Nieuwenhuisen, C. L. C., Hartog, H. S. Ph., and Matthijssen, E., 128*
Vascular system, disease of, review of, 504*
peripheral, action of nicotinic acid on, 697
disease of, 517 (B. rev.)
disorders of, intermittent venous compression in, treatment of, 255*
Vasocillator, Sander's, treatment of occlusive arterial disease of legs by, 312

Veins, compression, intermittent of, in treatment of peripheral vascular disorders, 255*
superficial, pattern of, infrared photographic demonstration of in congenital heart disease with cyanosis, 282
Vena cava, superior, observations of, syndrome of, 318
sclerosis of, in chronic congestive heart failure, 379*
Ventricle, asynchronism of, in bundle branch block, 126*
fibrillation of, method for study of, 363
left, failure of, differentiation of, from bronchial asthma by circulation time and other criteria, 765*
new sign of, 378*
tachycardia of, with variform ventricular complexes, 124*
paroxysmal of, 507*
Vitamin B_1, use of in rest pain of ischemic origin, 254*
Vogt, Elkin, Hamilton, W. F., and Woodbury, R. A., 122*
Volini, Italo F., and Flaxman, N., 510*

W

Wakim, Khalil G., Essex, H. E., and Mann, F. C., 171
Wall, Harry C., 228
Waller, John V., Katzin, H. M., and Blumgart, H. L., 638*
Watson, F., O'Shaughnessy, L., and Slome, D., 514*
Wave, Q_3, duration of, significance of, with respect to coronary disease, 309
QRS, second positive wave of, in Lead III, significance of electrocardiogram showing, 337*
Weissberg, Jonas, and Scherf, D., 411
Welty, J. W., 248*
White, Paul D., and Comeau, W. J., 334
—, and Graybiel, A., 122*
—, Mallory, G. K., and Salcedo-Salgar, J., 647
Wiggers, C. J., Wright, G. W., and Hallaran, W. R., 123*
Wilcox, Herbert B., Jr., and Andrus, E. C., 244*
Wilensky, Nathan D., and Collens, W. S., 517
Wilhelmy, E. W., and Helwig, F. C., 765*
Williams, Conger, 753
Williams, Denis, and Lennox, W. G., 767*
Williams, J. R., Jr., Harrison, T. R., and Brollman, A., 249*
Willius, Frederick A., and Dry, T. J., 765*
Winkler, Alexander W., Smith, P. K., and Hoff, H. E., 505*
Witsch, F., and Schlomka, G., 629*
Wolf, I. J., and Levinsohn, S. A., 241
Wood, J. Edwin, Jr., and Cash, J. R., 767*
Wood, Paul, and Selzer, A., 125*, 378*
Woodbury, R. A., Hamilton, W. F., and Vogt, E., 122*
—, Robinow, M., and Hamilton, W. F., 130*
Work, John L., and Garvin, C. F., 747
Wosika, P. H., and Maher, C. C., 511*
Wright, G. W., Hallaran, W. R., and Wiggers, C. J., 123*
Wright, Irving S., Fisher, M. M., and Duryee, A. W., 425
Wuhrmann, F., and Burger, R., 376*
Wullenweber, G., 248*

X

Xanthomatosis, hereditary, angina pectoris in, 633*

Y

Yater, Wallace M., 471

Z

Zazeela, Herman, Abramson, D. I., and Oppenheimer, B. S., 290
Zothe, H., 245*
Zweifach, Benjamin William, 248*
Zwemer, R. L., Chamberlain, F. L., and Scudder, J., 458

INDEX NUMBER

Vol. 18 DECEMBER, 1939 No. 6

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CONTENTS ON INSIDE COVER

The American Heart Journal

CONTENTS FOR DECEMBER, 1939

Original Communications

The Speed of Healing of Myocardial Infarction. G. Kenneth Mallory, M.D., and Paul D. White, M.D., Boston, Mass., and Jorge Salcedo-Salgar, M.D., Bogota, Colombia ---- 617

Combined Syphilitic Aortitis and Rheumatic Disease of the Heart. Homer Swanson, M.D., Nashville, Tenn. ---- 672

The Earliest Correlation of Clinical and Experimental Auricular Fibrillation. Malcolm Block, A.B., M.D., Ann Arbor, Mich. ---- 684

The Electrocardiogram in the Aged. George Levitt, M.D., St. Paul, Minn. 692

Nicotinic Acid: Its Action on the Peripheral Vascular System. Roy J. Popkin, M.D., Los Angeles, Calif. ---- 697

The Incidence of Organic Heart Disease in School Children. Louise W. Rauh, M.D., Cincinnati, Ohio ---- 705

A Comparative Study of Precordial Leads IV R and IV F. Arthur J. Geiger, M.D., New Haven, Conn. ---- 715

Roentgenkymography of the Heart. Richard Gubner, M.D., J. Hamilton Crawford, M.D., Wilbur A. Smith, M.D., and Harry E. Ungerleider, M.D., New York, N. Y. ---- 729

Coronary Embolism. Curtis F. Garvin, M.D., and John L. Work, M.D., Cleveland, Ohio ---- 747

Department of Clinical Reports

Bacterial Endocarditis Due to the Streptococcus Fecalis. Conger Williams, M.D., Boston, Mass. ---- 753

The Cardiac Mechanism in a Fatal Case of Acute Thyrotoxicosis. Alfred W. Harris, M.D., Dallas, Texas, Francis F. Rosenbaum, M.D., and Albert C. England, Jr., M.D., Boston, Mass. ---- 759

Department of Reviews and Abstracts

Selected Abstracts ---- 765

American Heart Association, Inc. ---- 774

Index ---- 775

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